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(54) Title: **MELANOCORTIN-4 RECEPTOR BINDING COMPOUNDS AND METHODS OF USE THEREOF**

(57) Abstract: MC4-R binding compounds of the formula: B-Z-E (I) wherein B is an anchor moiety, Z is a central moiety, and E is a MC4-R interacting moiety are discussed. Methods of using the compounds to treat MC4-R associated disorders, such as disorders associated with weight loss, are also discussed.

MELANOCORTIN-4 RECEPTOR BINDING COMPOUNDS AND METHODS OF USE THEREOF

Related Applications

5 This application claims priority to U.S. Patent Application Serial No. 09/778,468, entitled "Melanocortin-4 Receptor Binding Compounds and Methods of Use Thereof," filed on February 7, 2001, which is a continuation-in-part of U.S. Patent Application Serial No. 09/632,309, entitled "Melanocortin-4 Receptor Binding Compounds and Methods of Use Thereof," filed on August 4, 2000; which claims
10 priority to U.S. Provisional Application Serial No. 60/223,277, entitled "Melanocortin-4 Receptor Binding Compounds and Methods of Use Thereof," filed on August 3, 2000; and U.S. Provisional Application Serial No. 60/147,288, entitled "Melanocortin-4 Receptor Binding Compounds and Methods of Use Thereof," filed on August 4, 1999; the entire contents of all of the aforementioned applications are hereby incorporated
15 herein by reference.

Background

 Melanocortins are known to have a broad array of physiological actions (Nakanishi, et al. *Nature* (1979) 278:423-427). Aside from their well known effects on
20 adrenal cortical functions and on melanocytes, melanocortins have been shown to affect behavior, learning, memory, control of the cardiovascular system, analgesia, thermoregulation, and the release of other neurohumoral agents including prolactin, luteinizing hormone, and biogenic amines (De Weid et al. *Methods Achiev. Exp. Pathol.* (1991) 15:167-199; De Weid et al. *Physiol. Rev.* (1982) 62:977-1059; Gruber, K.A. et
25 al. *Am. J. Physiol.* (1989) 257:R681-R694; Murphy et al. *Science* (1980) 210:1247-1249; Murphy et al. *Science* (1983) 221:192-193; Ellerkmann, E. et al. *Endocrinol.* (1992) 130:133-138; Versteeg, D.H.G. et al. *Life Sci.* (1986) 835-840). Peripherally, melanocortins have been identified to have immunomodulatory and neurotrophic properties, and to be involved in events surrounding parturition (Cannon, J.G. et al. *J.*
30 *Immunol.* (1986) 137:2232-2236; Gispen, W.H. *Trends Pharm. Sci.* (1992) 11:221-222; Wilson, J.F. *Clin. Endocrinol.* (1982) 17:233-242; Clark, D. et al. *Nature* (1978) 273:163-164; Silman, R.E. et al. *Nature* (1976) 260:716-718). Furthermore, melanocortins are present in a myriad of normal human tissues including the brain, ovary, lung, thyroid, liver, colon, small intestine and pancreas (Tatro, J.B. et al.
35 *Endocrinol.* (1987) 121:1900-1907; Mountjoy, K.G. et al. *Science* (1992) 257:1248-1251; Chhajlani, V. et al., *FEBS Lett.* (1992) 309:417-420; Gantz, L. et al., *J. Biol. Chem.* (1993) 268:8246-8250; Gantz, L. et al., *J. Biol. Chem.* (1993) 268:15174-15179).

Recent studies have described an unexpected diversity of subtypes of receptors for the melanocortin peptides and determined that they belong to the superfamily of seven transmembrane G-protein linked cell surface receptors (Mountjoy, K.G. et al., *Science*(1992), *supra*; Chhajlani, V. et al., *FEBS Lett.* (1992), *supra*). Five melanocortin
5 receptor subtypes have been cloned. The melanocortin-1 (MC1) receptor is found in melanoma cells, where it has a role in mediating pigmentation. The melanocortin-2 receptor (MC2-R or ACTH receptor) is found in the adrenal glands where it mediates the effects of ACTH (adrenocorticotrophic hormone). The melanocortin-3 receptor (MC3-R) is primarily found in the central nervous system (CNS) (Gantz, L. et al., *J.*
10 *Biol. Chem.* (1993) 268:8246-8250), but its physiological function is still unknown. The melanocortin-4 receptor (MC4-R) has been found in the brain, where it is widely distributed in several areas, including the cortex, thalamus, hypothalamus, brain stem, and spinal cord (Gantz, L. et al. *J. Biol. Chem.* (1993) 268:15174-15179; Mountjoy, K.G. et al. *Mol. Endocrinol.* (1994) 8:1298-1308). MC4-R has recently been related to
15 weight homeostasis. MC4-R "knock out" mice have been shown to develop obesity (Huszar et al. *Cell* (1997) 88:131-141). The feeding behavior leading to the obesity can be inhibited by injection of MSH peptides (Vergoni et al. *Neuropeptides* (1986) 7:153-158; Vergoni et al. *Eur. J. Pharmacol.* (1990) 179:347-355; Fan et al. *Nature* (1997) 385:165-168). The melanocortin-5 receptor (MC5-R) has a wide peripheral distribution
20 and is believed to participate in the regulation of the exocrine gland function (Chen et al. *Cell* (1997) 91:789-798).

Summary

In one aspect, the invention pertains to a method for treating a melanocortin-4
25 receptor (MC4-R) associated state in a mammal. The method involves administering an effective amount of a MC4-R binding compound to a mammal, such that the MC4-R associated state is treated. The MC4-R binding compound is of the formula (I):



30

wherein B is an anchor moiety, Z is a central moiety, E is a MC4-R interacting moiety, and pharmaceutically acceptable salts, thereof.

In a further embodiment, the MC4-R binding compound is of the formula (II):



35

wherein B is an anchor moiety, A is cyclic moiety, E is a MC4-R interacting moiety, and pharmaceutically acceptable salts, thereof.

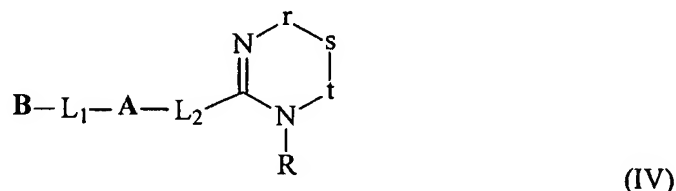
In another embodiment, the invention pertains to another method for treating an MC4-R associated state in a mammal, by administering to a mammal an effective
5 amount of a MC4-R binding compound of formula (III):



wherein B is an anchor moiety, L₁ and L₂ are linking moieties, A is a cyclic moiety, E is
10 a MC4-R interacting moiety, and pharmaceutically acceptable salts thereof.

The invention also pertains to treating MC4-R associated states with an MC4-R binding compound of formula III, wherein B is substituted or unsubstituted biaryl, unsubstituted or substituted heterocyclic, or unsubstituted or substituted phenyl, wherein one or more of said substituents are halogens, hydroxy, alkyl, alkynyl, alkoxy, aryl,
15 amino, cyano, or nitro; L₁ is a covalent bond, C₁-C₁₀ branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms; L₂ is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl; E is substituted or unsubstituted alkyl, amino, amidino, guanidino, heterocyclic, or aryl, wherein said substituents are amino, arylalkyl, aminoalkyl, alkyl,
20 aryl, alkenyl, or alkynyl; and A is a substituted or unsubstituted phenyl, heteroaryl, cycloalkyl, or biaryl, and pharmaceutically acceptable salts thereof.

In another embodiment, the invention pertains to a method for treating an MC4-R associated state in a mammal by administering an effective amount of a MC4-R binding compound to a mammal, such that the MC4-R associated state is treated. In this
25 embodiment, the compound is of the formula (IV):

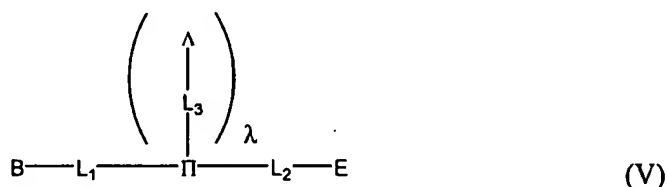


wherein B is substituted or unsubstituted alkyl, cycloalkyl, alkenyl, alkynyl, aryl, or heteroaryl; A is aryl, heteroaryl, biaryl, cycloalkyl, heterocyclic, or cycloalkenyl; L₁ and L₂ are selected from the group consisting of a covalent bond, C₁-C₆ branched or
30 unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms; r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H; t is CH, CH₂, CHR³, CR³R⁴, or H; s is CHR⁵, CR⁵, CR⁵R⁶ or absent (e.g., leaving a non-cyclic diamine); R is H, substituted or unsubstituted alkyl, arylalkyl, or heteroalkyl, and may optionally be linked to A, B, L₁, or L₂; R¹, R², R³, R⁴, R⁵, and R⁶ are each

substituted or unsubstituted alkyl, alkenyl, halogen, thiol, thioether, thioalkyl, or alkoxy, and may optionally be linked to form a carbocyclic or heterocyclic ring.

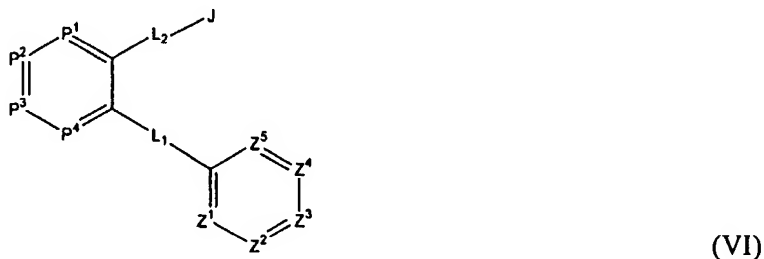
Pharmaceutically acceptable salts of the MC4-R binding compound are also included.

- The invention also pertains to methods for treating an MC4-R associated state in a mammal by administering an effective amount of a MC4-R binding compound of the formula (V):



- wherein B is substituted or unsubstituted biaryl, unsubstituted or substituted heterocyclic, or unsubstituted or substituted phenyl, wherein one or more of said substituents are halogens, alkyl, alkynyl, alkoxy, aryl, amino, cyano, or nitro; L₁ is a covalent bond, C₁-C₁₀ branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms; L₂ is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl; E is substituted or unsubstituted alkyl, amino, amidino, guanidino, heterocyclic, or aryl, wherein said substituents are amino, arylalkyl, aminoalkyl, alkyl, aryl, alkenyl, or alkynyl; Π is a covalent bond, a carbon atom, a nitrogen atom, heterocyclic, alkyl, cycloalkyl, or aryl; L₃ is a covalent bond, C₁-C₆ branched, unbranched or cyclic alkyl, wherein one, two or three of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms, carbonyl, aminocarbonyl, aminocarbonylamino, aminocarbonyloxy, or aminothiocarbonyl; and Λ is heterocyclic, aryl, alkoxy, amino, alkyl, alkenyl, alkynyl, or hydrogen; and λ is 0, 1 or 2, and pharmaceutically acceptable salts thereof.

- In yet another embodiment, the invention also pertains to a method for treating an MC4-R associated state in a mammal by administering an effective amount of a MC4-R binding compound to a mammal, wherein the compound is an MC4-R antagonist, and is of the formula (VI):

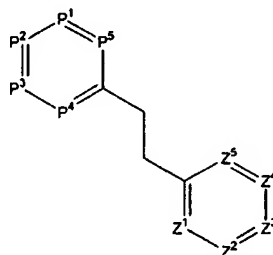


wherein

P^1 , P^2 , P^3 , and P^4 are optionally substituted carbon, sulfur, or nitrogen, and wherein one of P^1 , P^2 , P^3 and P^4 may represent a covalent bond; Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 are optionally substituted carbon or nitrogen; L_1 is a covalent bond, C_1 - C_{10} branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with
 5 oxygen, sulfur or nitrogen atoms; L_2 is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl; and J is an unsubstituted or substituted nitrogen containing heterocycle or a substituted or unsubstituted amino group, and pharmaceutically acceptable salts thereof.

In another embodiment, the MC4-R binding compound is of formula (VII):

10



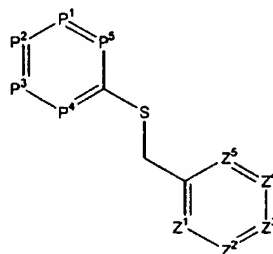
(VII)

wherein

Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 are CH, N, or substituted carbon; and
 P^1 , P^2 , P^3 , P^4 , and P^5 are CH, N or substituted carbon.

15

In another embodiment, the MC4-R binding compound is of formula (VIII):



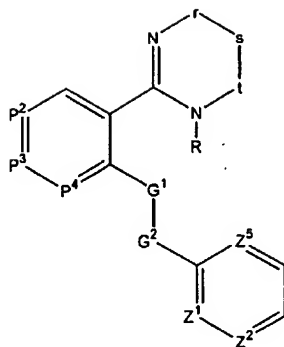
(VIII)

wherein

Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 are CH, N, or substituted carbon; and
 P^1 , P^2 , P^3 , P^4 , and P^5 are CH, N or substituted carbon.

20

The invention also pertains to MC4-R binding compound of the formula (IX):



(IX)

wherein:

- 5 P² is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or
 a covalent bond;
 P³ is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, or Cl;
 P⁴ is CH, CCl, CBr, CF, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or
 a sulfur atom;
 G¹ and G² are each independently CH₂, S, or O;
 10 r is a covalent bond or CH₂;
 t is CH₂, CHR³, or CR³R⁴;
 s is CH₂, CHR⁵ or CR⁵R⁶;
 R is hydrogen, alkyl, alkoxy, carbonyl, or alkylcarbonyl;
 Z¹ is CH, or covalently linked to Z² to form a naphthyl ring;
 15 Z² is CH, C-(C≡CH), CCl, CBr, Cl, CF, or covalently linked to Z¹ to
 form a naphthyl ring;
 Z⁵ is CH, C-alkoxy or C-OMe;
 R³, R⁴, R⁵, and R⁶ are methyl, ethyl, hydroxyl, alkoxy, halogen, cyano,
 nitro, or amino, or pharmaceutically acceptable salts thereof.

- 20 The invention also features a pharmaceutical composition for the treatment of a
 MC4-R associated state in a mammal. The pharmaceutical compositions contain a
 pharmaceutically acceptable carrier and a MC4-R binding compound. The compounds
 are described herein in the context of the description of the method but it should be
 understood that the invention further pertains to pharmaceutical compositions containing
 25 the compounds and the compounds *per se*. For example, pharmaceutical compositions
 of the invention include a pharmaceutically acceptable carrier and an effective amount
 of at least one MC4-R binding compound of the formula (I):

B-Z-E

(I)

30

wherein B is an anchor moiety, Z is an central moiety, E is a MC4-R interacting moiety, and pharmaceutically acceptable salts thereof.

Brief Description of the Drawings

5 Figures 1a and 1b are bar graphs showing the effects of MT II (a MC4-R agonist) on food intake in lean mice.

Figure 2 is a graph depicting the effects of treating lean mice with Compound N and MT II on food intake over a six hour period.

10

Figure 3 is a graph depicting the effects of treating lean mice with Compound O and MT II on food intake over a six hour period.

Detailed Description of the Invention

15 In one aspect, the invention pertains to a method for treating a melanocortin-4 receptor (MC4-R) associated state in a mammal. The method involves administering an effective amount of a MC4-R binding compound to a mammal, such that the MC4-R associated state is treated. The MC4-R binding compound is of the formula (I):

20

B-Z-E

(I)

wherein B is an anchor moiety, Z is a central moiety, E is a MC4-R interacting moiety, and pharmaceutically acceptable salts thereof.

25 The term "MC4-R" includes receptors for α -melanocyte stimulating hormone. The MC4-R is usually found in the brain where it is widely distributed (Mountjoy et al. *Mol. Endocrinol.* (1994) 8:1298-1308). Melanocortins are peptide hormones that play an important role in regulating melanocyte pigmentation as well as memory and thermoregulation. They consist of various peptides, such as α -melanocyte stimulating hormone, that are cleaved from the polypeptide precursor proopiomelanocortin (POMC). The effects of melanocortins are mediated via stimulation of adenylate cyclase via the activation of the melanocortin receptors.

30 The melancortin-4 receptor (MC4-R) is a G-protein coupled receptor (GPCR) expressed in brain tissue. The specific role of the MC4-R protein *in vivo* was investigated by engineering MC4-R "knock out" mice. The mice were unable to produce functional MC4-R protein, because the endogenous MC4-R gene coding sequence was deleted.

- The knock-out mice were produced by using human MC4-r gene sequences to isolate and clone the murine MC4-r gene. A murine MC4-r targeting construct was then generated which was designed to delete the majority of the murine MC4-r coding sequence upon homologous recombination with the endogenous murine MC4-r gene.
- 5 Embryonic stem (ES) cells containing the disrupted MC4-r gene were produced, isolated and microinjected into murine blastocysts to yield mice chimeric for cells containing a disrupted MC4-r gene. Offspring of the chimeric mice resulting from germline transmission of the ES genome were obtained and animals heterozygous for the disrupted MC4-R were identified.
- 10 To assess the role of MC4-R *in vivo*, the animals heterozygous for the MC4-r disrupted gene were bred together, producing litters containing wild-type mice, mice heterozygous for the MC4-r mutation and mice homozygous for the MC4-R mutation. The weight gain of the animals was monitored regularly. Homozygous null MC4-R mutants showed an increase in weight compared to mice heterozygous for MC4-R
- 15 deletion and wild type mice as early as 25 days of age. By 54-58 days of age, MC4-R deficient mice exhibited, on average, a 55-70% greater weight relative to wild type mice, and an approximately 50% greater weight compared to mice heterozygous for the MC4-R deletion.
- The language "MC4-R associated states" includes those states, disorders, or
- 20 diseases characterized by aberrant or undesirable activity or expression of MC4-Rs. It also includes those states, disorders and diseases associated with MC4-R ligands (e.g., α -melanocyte stimulating hormone). The language also includes prevention of states, disorders and diseases characterized by aberrant or undesirable activity of MC4-Rs or its ligands. Examples of MC4-R associated states include, but are not limited to, disorders
- 25 involving or associated with pigmentation, bones, and weight homeostasis, e.g., weight loss or obesity. MC4-R associated states include the unhealthy decrease in body weight that can occur during an acute inflammatory response or that occurs in a cancer patient as a result of cachexia, radiotherapy or chemotherapy, or to the undesirable decrease in body mass due to simulated or actual weightlessness, such as occurs during space travel.
- 30 Other examples of unhealthy decreases in weight occur in some patients during advance stages of illnesses such as AIDS. Physiologically, this may be a result from any one of a number of complex factors, such as loss of appetite and possibly abnormal catabolism. This cachexia, may be slowed by MC4-R binding compounds. In a preferred embodiment of the invention, the weight loss is a result of old age, anorexia
- 35 nervosa, or cachexia (e.g., cachexia associated with cancer or HIV).

In one further embodiment, the MC4-R associated state is not weight loss.

In an embodiment, the MC4-R associated disorder is a bone associated disorder. MC4-R knockout mice have been shown to have enhanced bone thickness (Ducy *et al. Science*, (Sept., 2000) 289:1501-1504). Examples of bone associated disorders which
5 may be treated with MC4-R binding compounds of the invention include disorders and states where the formation, repair or remodeling of bone is advantageous. For examples bone associated states include osteoporosis (e.g., a decrease in bone strength and density), bone fractures, bone formation associated with surgical procedures (e.g., facial reconstruction), osteogenesis imperfecta (brittle bone disease), hypophosphatasia,
10 Paget's disease, fibrous dysplasia, osteopetrosis, myeloma bone disease, and the depletion of calcium in bone, such as that which is related to primary hyperparathyroidism. Bone associated disorders include all states in which the formation, repair or remodeling of bone is advantageous to the subject as well as all other disorders associated with the bones or skeletal system of a subject which can be
15 treated with the compounds of the invention.

The term "mammal" includes organisms which express the MC4-R. Examples of mammals include mice, rats, cows, sheep, pigs, goats, horses, bears, monkeys, dogs, cats and, preferably, humans. Transgenic organisms which express the MC4-R are also included in this definition.

20 The language "MC4-R binding compound" includes those compounds which interact with the MC4-R resulting in modulation of the activity of the MC4-R. In an embodiment, the MC4-R binding compounds are antagonists of the MC4-R. The term "antagonist" includes compounds which interact with the MC4-R and modulate, e.g., inhibit or decrease, the ability of a second compound, e.g., α -melanocyte stimulating
25 hormone or another MC4-R ligand, to interact with the MC4-R. In another embodiment, the MC4-R binding compounds is an agonist of the MC4-R. The term "agonists" includes compounds which interact with the MCR-4 and modulate, e.g., increase or stimulate, its activity and/or its ability to interact with a second compounds, e.g., α -melanocyte stimulating hormone.

30 MC4-R binding compounds can be identified through both *in vitro* (e.g., cell and non-cell based) and *in vivo* methods. These methods are described in detail in Examples 2, 3, 4, and 5.

The Scintillation Proximity Assay (SPA) is a non-cell based *in vitro* assay, described in Example 2. It can be used to identify compounds that interact with, e.g.,
35 bind to MC4-R. Such compounds may act as antagonists or agonists of MC4-R activity and may be used in the treatment of body weight disorders. One example of a qualitative measure of binding affinity of a MC4-R binding compound to MC4-R is its IC_{50} . Preferably, the MC4-R binding compound binds to the MC4-R with a binding

affinity, for example, of about 50 μ M or less, 20 μ M or less, 10 μ M or less, 5 μ M or less, 2.5 μ M or less, or 1 μ M or less. In an advantageous embodiment, the IC₅₀ of a MC4-R binding compounds is about 0.5 μ M or less, about 0.3 μ M or less, about 0.1 μ M or less, about 0.08 μ M or less, about 0.06 μ M or less, about 0.05 μ M or less, about 0.04 μ M or less, or, preferably, about 0.03 μ M or less.

In the SPA, isolated membranes are used to identify compounds that interact with MC4-R. For example, in a typical experiment using isolated membranes, 293 cells may be genetically engineered to express the MC4-R. Membranes are harvested by standard techniques and used in an *in vitro* binding assay. ¹²⁵I-labeled ligand (e.g., ¹²⁵I-labeled α -MSH, β -MSH, or ACTH) is bound to the membranes and assayed for specific activity; specific binding is determined by comparison with binding assays performed in the presence of excess unlabelled ligand.

To identify MC4-R binding compounds, membranes are incubated with labeled ligand in the presence or absence of test compound. Compounds that bind to the receptor and compete with labeled ligand for binding to the membranes reduced the signal compared to the vehicle control samples. Preferably, the screens are designed to identify compounds that antagonize the interaction between MC4-R and MC4-R ligands such as α -MSH, β -MSH and ACTH. In such screens, the MC4-R ligands are labeled and test compounds can be assayed for their ability to antagonize the binding of labeled ligand to MC4-R.

Cell based assay systems can also be used to identify MC4-R binding compounds. An example of a cell based assay system is the cAMP assay described in detail in Example 3. Cell based methods may use cells that endogenously express MC4-R for screening compounds which bind to MC4-R. Alternatively, cell lines, such as 293 cells, COS cells, CHO cells, fibroblasts, and the like, genetically engineered to express the MC4-R can also be used for screening purposes. Preferably, host cells genetically engineered to express a functional receptor that responds to activation by melanocortin peptides can be used as an endpoint in the assay; e.g., as measured by a chemical, physiological, biological, or phenotypic change, induction of a host cell gene or a reporter gene, change in cAMP levels, adenylyl cyclase activity, host cell G protein activity, extracellular acidification rate, host cell kinase activity, proliferation, differentiation, etc.

To be useful in screening assays, the host cells expressing functional MC4-R should give a significant response to MC4-R ligand, preferably greater than 5-fold induction over background. Host cells should preferably possess a number of characteristics, depending on the readout, to maximize the inductive response by melanocortin peptides, for example, for detecting a strong induction of a CRE reporter gene: (a) a low natural level of cAMP, (b) G proteins capable of interacting with the

MC4-R, (c) a high level of adenylyl cyclase, (d) a high level of protein kinase A, (e) a low level of phosphodiesterases, and (f) a high level of cAMP response element binding protein would be advantageous. To increase response to melanocortin peptide, host cells could be engineered to express a greater amount of favorable factors or a lesser amount of unfavorable factors. In addition, alternative pathways for induction of the CRE reporter could be eliminated to reduce basal levels.

In using such cell systems, the cells expressing the melanocortin receptor are exposed to a test compound or to vehicle controls (e.g., placebos). After exposure, the cells can be assayed to measure the expression and/or activity of components of the signal transduction pathway of the melanocortin receptor, or the activity of the signal transduction pathway itself can be assayed. For example, after exposure, cell lysates can be assayed for induction of cAMP. The ability of a test compound to increase levels of cAMP, above those levels seen with cells treated with a vehicle control, indicates that the test compound induces signal transduction mediated by the melanocortin receptor expressed by the host cell. In screening for compounds that may act as antagonists of MC4-R, it is necessary to include ligands that activate the MC4-R, e.g., α -MSH, β -MSH or ACTH, to test for inhibition of signal transduction by the test compound as compared to vehicle controls.

When it is desired to discriminate between the melanocortin receptors and to identify compounds that selectively agonize or antagonize the MC4-R, the assays described above may be conducted using a panel of host cells, each genetically engineered to express one of the melanocortin receptors (MC1-R through MC5-R). Expression of the human melanocortin receptors is preferred for drug discovery purposes. To this end, host cells can be genetically engineered to express any of the amino acid sequences shown for melanocortin receptors 1 through 5. The cloning and characterization of each receptor has been described: MC1-R and MC2-R (Mountjoy., 1992, Science 257: 1248-1251; Chhajlani & Wikberg, 1992 FEBS Lett. 309: 417-420); MC3-R (Roselli-Rehfuss et al., 1993, Proc. Natl. Acad. Sci., USA 90: 8856-8860; Gantz et al., 1993, J. Biol. Chem. 268: 8246-8250); MC4-R (Gantz et al., 1993, J. Biol. Chem. 268: 15174-15179; Mountjoy et al., 1994, Mol. Endo. 8: 1298-1308); and MC5-R (Chhajlani et al., 1993, Biochem. Biophys. Res. Commun. 195: 866-873; Gantz et al., 1994, Biochem. Biophys. Res. Commun. 200: 1234-1220), each of which is incorporated by reference herein in its entirety. Thus, each of the foregoing sequences can be utilized to engineer a cell or cell line that expresses one of the melanocortin receptors for use in screening assays described herein. To identify compounds that specifically or selectively regulate MC4-R activity, the activation, or inhibition of MC4-R activation is compared to the effect of the test compound on the other melanocortin receptors. In certain embodiments, it may be advantageous to select compounds of the

invention selective for MC4-R, or, alternatively, it may be useful to select compounds which interact with other receptors as well.

In one further embodiment, the MC4-R binding compounds of the invention are more selective for the MC4-R than at least one other MC receptors, for example, more
5 than twice as selective, at least ten times as selective, at least twenty times as selective, at least fifty times as selective, or at least one hundred times as selective.

In one further embodiment, the MC4-R binding compounds of the invention are more selective for the MC4-R than the MC1-R, for example, more than twice as selective, at least ten times as selective, at least twenty times as selective, at least fifty
10 times as selective, or at least one hundred times as selective.

In one further embodiment, the MC4-R binding compounds of the invention are more selective for the MC4-R than the MC3-R, for example, more than twice as selective, at least ten times as selective, at least twenty times as selective, at least fifty times as selective, or at least one hundred times as selective.

15 In one further embodiment, the MC4-R binding compounds of the invention are more selective for the MC4-R than the MC5-R, for example, more than twice as selective, at least ten times as selective, at least twenty times as selective, at least fifty times as selective, or at least one hundred times as selective.

In yet another further embodiment, the MC4-R binding compounds of the invention are more selective for the MC4-R receptor than at least one, two or three other
20 MC receptors (such as, for example, MC1-R, MC3-R, or MC5-R). In a further embodiment, the MC4-R binding compounds are more selective for the MC4-R than MC1-R, MC3-R, and MC5-R. In a further embodiment, the MC4-R binding compounds as at least ten times as selective, at least twenty times as selective, at least fifty times as
25 selective, or at least one hundred times as selective for the MC4-R than the MC1-R, MC3-R and the MC5-R.

As stated above, in an embodiment, the MC4-R binding compound includes compounds of the formula (I):

30

B-Z-E

(I)

wherein B is an anchor moiety, Z is a central moiety, E is a MC4-R interacting moiety, and pharmaceutically acceptable salts thereof.

35 The language "anchor moiety" ("B") includes moieties which interact with the MC4-R, which may, advantageously, result in the binding of the MC4-R binding compound to the MC4-R. Examples of anchor moieties include substituted or unsubstituted alkyl (e.g., branched, straight chain, or cyclic (e.g., cyclohexane,

cyclopentane)), alkenyl, alkynyl, aryl (e.g., substituted or unsubstituted phenyl, naphthyl, biphenyl, anthracenyl, fluorenyl, etc.), heterocyclic (e.g., thienyl, morpholinyl, piperazinyl, piperidinyl, etc.), and multicyclic (e.g., indolyl, benzothienyl, etc.) moieties. Other examples of anchor moieties include carbonyl moieties, thiol groups, cyano
 5 groups, amino groups, and hydrogen atoms.

In a further embodiment, the anchor moiety ("B") includes substituted or unsubstituted carbocyclic aryl moieties, e.g., phenyl, naphthyl, etc. Examples of substituents include halogens (e.g., fluorine, chlorine, iodine, bromine, etc.), alkoxy (e.g., methoxy, ethoxy, isopropoxy, n-propyloxy, n-butyloxy, pentoxy, cyclopentoxo,
 10 arylalkyloxy, etc.) hydroxy, alkylcarbonyl, cyano, nitro, thiol, thioether, thioalkyl, alkenyl, alkynyl (e.g., ethynyl, etc.), alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including
 15 alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, trifluoromethyl, azido, heterocyclyl, alkylaryl, heteroaryl, alkyl (e.g., unsubstituted (e.g., methyl, ethyl, propyl, butyl, hexyl, etc.) or substituted, e.g., halogen substituted, e.g., trifluoromethyl, trichloromethyl), aryl (e.g., substituted and
 20 unsubstituted phenyl, heteroaryl (e.g., thienyl, pyridinyl, etc.), arylalkyl, arylalkenyl, arylalkynyl, or combinations thereof. In yet another further embodiment, the anchor moiety substituent can be substituted itself with one or more halogen, nitro, alkyl, alkenyl, alkynyl, aryl or alkoxy groups, or combinations thereof. In certain embodiments, the aryl moiety is fused to another ring which can be substituted or
 25 unsubstituted, carbocyclic or heterocyclic, aromatic or non-aromatic.

In a further embodiment, the anchor moiety is substituted with at least one halogen, alkoxy group, or alkyl (e.g., substituted or unsubstituted) group. Examples of halogen substituted phenyl anchor moieties include *o*-iodophenyl, *m*-iodophenyl, *o*-bromophenyl, *m*-bromophenyl, *o*-chlorophenyl, *m*-chlorophenyl, *o*-fluorophenyl, *m*-fluorophenyl, *p*-fluorophenyl, *m*-nitrophenyl, or *o*-methoxy. The anchor moiety may
 30 also comprise more than one substituent, e.g. two halogens, e.g., two fluorines, a fluorine and a chlorine. Other examples of anchor moieties include 2-methoxy-5-bromophenyl, 2-methoxy-5-fluorophenyl, 2-methoxy-5-iodophenyl, 2-methoxy-5-fluorophenyl, 2-ethoxy-5-bromophenyl, 2-methoxy-6-bromophenyl, 3-methoxy-6-bromophenyl, 2-isopropyl-5-bromophenyl, 2-*n*-propyl-5-bromophenyl, and 2-cyclopentyloxy-5-bromophenyl.
 35

Other examples of anchor moieties include, but are not limited to, 2-methoxy-5-cyanophenyl, 2-chloro-5-chlorophenyl, 2-methoxy-6-methoxyphenyl, 2-methoxy-5-nitrophenyl, 2-methoxy-5-phenyl phenyl, 2-methoxy-5-3'-thiofuranyl phenyl, 2-methoxy-5-methylcarbonyl phenyl, 3,5-dimethoxy phenyl, 2-methoxyphenyl, 2,5-dimethoxy phenyl, 2-fluoro-6-chlorophenyl, and 3-chloro-4-fluorophenyl.

In another further embodiment, the anchor moiety includes substituted and unsubstituted heterocycles. Examples of such heterocycles include, but are not limited to, furanyl, imidazolyl, benzothiophenyl, benzofuranyl, quinolinyl, isoquinolinyl, benzodioxanyl, benzoxazolyl, benzothiazolyl, methylenedioxyphenyl, ethylenedioxyphenyl, indolyl, thienyl, pyrimidyl, pyrazinyl, purinyl, deazapurinyl, morpholine, piperazine, piperidine, thiomorpholine, and thioazolidine. Examples of substituents include alkyl (e.g., substituted or unsubstituted, branched straight chain or cyclic, e.g., methyl, ethyl, propyl, butyl, pentyl, etc.), alkenyl, alkynyl, halogens (e.g., fluorine, chlorine, bromine, iodine, etc.), hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylaryl amino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, azido, heterocyclyl, alkylaryl, aryl and heteroaryl groups.

In another further embodiment, the anchor moiety ("B") is a substituted or unsubstituted fused aryl or biaryl moiety. Biaryl moieties include moieties with two or more aromatic rings, which may be fused or connected through one or more covalent bonds. Examples include biphenyl, fluorene, anthracenyl, benzoquinazolinyl, and naphthyl. Examples of substituents of biaryl moieties include alkyl (e.g., substituted and unsubstituted, branched or straight chain, methyl, ethyl, propyl, butyl, pentyl, etc.), alkoxy (e.g., methoxy, ethoxy, propoxy, butoxy, pentoxy, cyclopentoxy, etc.), alkenyl, alkynyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylaryl amino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, an aromatic heteroaromatic moiety, halogens (e.g., fluorine, chlorine, bromine, iodine, etc.), combinations thereof and other groups which allow the MC4-R binding compound to perform its intended function. Biaryl moieties also include moieties which comprise one

or more heterocycles, such as, benzothiofuranyl, benzothienyl, quinolinyl, benzothiophenyl, benzofuranyl, isoquinolinyl, benzodioxanyl, benzoxazolyl, benzothiazolyl, methylenedioxyphenyl, ethylenedioxyphenyl, and indolyl. Examples of biaryl anchor moieties include naphthyl, 2-methoxynaphthyl, 2-methoxy-5-phenyl
 5 phenyl, 2-ethoxynaphthyl, 2-methoxy-5-thiofuranyl phenyl, 2-methyl naphthyl, 2-n-propyl naphthyl, benzothiofuranyl, 2-phenyl phenyl, 2-methoxy-5-4'-methoxy-phenyl phenyl; 2-methoxy-5-(3'-fluoro-4'-phenyl) phenyl phenyl; 2-cyclopentoxynaphthyl; quinolinyl; and 2-methoxy-5-(3'-chloro-4'-fluoro)phenyl phenyl.

Furthermore, the anchor moiety can be multicyclic and comprise a combination
 10 of one or more aromatic, non-aromatic, heterocyclic, and heteroaryl rings, which can be fused, bridged, or linked together through covalent bonds. The multicyclic anchor moiety may also be substituted with substituents such as alkyl (e.g., substituted or unsubstituted, branched straight chain or cyclic, e.g., methyl, ethyl, propyl, butyl, pentyl, etc.), alkenyl, alkynyl, halogens (e.g., fluorine, chlorine, bromine, iodine, etc.),
 15 hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonate, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino,
 20 imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, azido, heterocyclyl, alkylaryl, aryl and heteroaryl groups.

The term "central moiety" ("Z") includes moieties which covalently attach the anchor moiety to the MC4-R interacting moiety. Examples of central moieties include
 25 cyclic moieties, optionally substituted amines (e.g., tertiary amino, aminoalkylamino, dialkylaminoalkylamino, aminocarbonylamino, aminocarbonylamino; arylaminocarbonylamino groups; arylaminothiocarbonylamino), optionally substituted alkyl groups (e.g., carbon atoms with substituted or unsubstituted alkyl, aryl (e.g., phenyl, naphthyl), heterocyclic moieties (e.g., morpholinyl, piperazinyl, etc.), and
 30 carbonyl groups, etc. Examples of substituents of the central moiety include, for example, alkyl (e.g., straight, branched or cyclic, substituted or unsubstituted, methyl, ethyl, propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl), alkenyl (ethenyl, propenyl, butenyl, etc.), alkynyl (e.g., ethynyl, propynyl, etc.), halogen (e.g., chlorine, fluorine, iodine, bromine), hydroxyl, alkoxy (e.g., methoxy, ethoxy, trifluoromethoxy, trichloromethoxy, propoxy, butoxy, cyclopropoxy, etc.), alkylcarbonyloxy,
 35 arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonate, phosphinato, cyano, amino (including alkyl amino, arylalkylamino, dialkylamino,

arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, azido, heterocyclyl (e.g., morpholinyl, piperazinyl, etc.), arylalkyl, alkylaryl and aryl (e.g., substituted or unsubstituted phenyl (e.g., alkyl, halogen, alkoxy substituted), naphthyl, anthracene, etc.) and heteroaryl moieties. Furthermore, the central moiety may further comprise one or more linking moieties. For example, the linking moieties may covalently link the cyclic moiety to the anchor moiety and/or the MC4-R interacting moiety.

The term "central moiety" also includes moieties of the formula (XII):



wherein

Π is a covalent bond, a carbon atom, a nitrogen atom, heterocyclic, alkyl, carbocyclic, or aryl;

L_3 is a covalent bond, C_1 - C_6 branched, unbranched or cyclic alkyl (wherein one, two or three of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms), carbonyl, aminocarbonyl, aminocarbonylamino, aminocarbonyloxy, or aminothiocarbonyl moiety;

Λ is substituted or unsubstituted heterocyclic, aryl, alkoxy, amino, alkyl, alkenyl, alkynyl, or hydrogen; and

λ is 0, 1 or 2.

In a further embodiment, Π is a carbon or nitrogen atom. In other embodiments, Π is alkyl, carbocyclic, heterocyclic (e.g., piperazinyl, morpholinyl, piperidinyl, etc.).

In another further embodiment, Λ is heterocyclic (e.g., non-aromatic, e.g., substituted or unsubstituted, bridged, fused, or monocyclic, morpholinyl, piperidinyl, azetidiny, piperazinyl, etc. or aromatic, e.g., pyridinyl, pyrimidinyl, pyrrolyl, etc.), aryl e.g., phenyl, naphthyl) or amino (e.g., substituted or unsubstituted, e.g., alkylamino, dialkyl amino, etc.).

The language "cyclic moiety" includes heterocyclic and carbocyclic groups, such as substituted or unsubstituted phenyl, heteroaryl, or biaryl moieties. Examples of cyclic moieties include those without aromaticity (e.g., cyclohexane, cyclopentane, etc.) and those with aromaticity, e.g. moieties that have at least one aromatic ring. Cyclic moieties may include one or more heteroatoms. Examples include phenyl, pyrrole, furan, thiophene, imidazole, benzoxazole, benzothiazole, triazole, tetrazole, pyrazole,

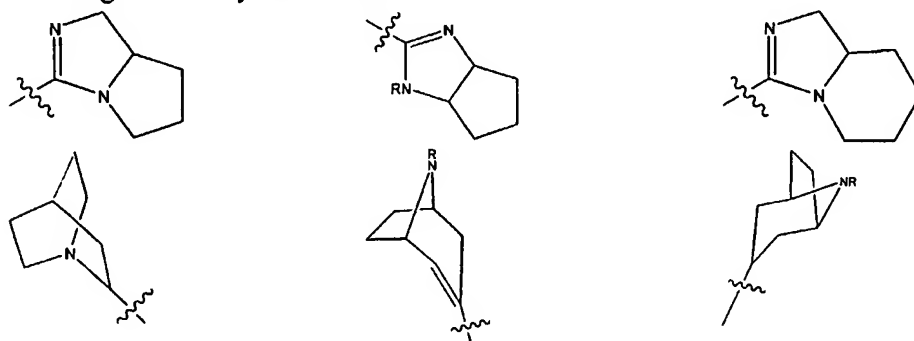
pyridine, pyrazine, pyridazine, pyrimidine, naphthyl, quinolyl, indolyl, and the like. The cyclic moiety can be substituted at one or more ring positions with such substituents such as, for example, alkyl (e.g., substituted or unsubstituted methyl, ethyl, propyl, butyl), alkenyl (ethenyl, propenyl, butenyl, etc.), alkynyl (e.g., ethynyl, propynyl, etc.),
5 halogen (e.g., chlorine, fluorine, iodine, bromine), hydroxyl, alkoxy (e.g., methoxy, ethoxy, trifluoromethoxy, trichloromethoxy, propoxy, butoxy, cyclopropoxy, etc.), aryloxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxy carbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino,
10 dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, azido, heterocyclyl, alkylaryl, and aryl (e.g., substituted or unsubstituted phenyl, naphthyl) and heteroaryl moieties. The cyclic
15 moiety can also be fused or bridged with alicyclic or heterocyclic rings which are not aromatic so as to form a polycycle (e.g., tetralin, or fluorene).

In an embodiment, the cyclic moiety of the present invention is substituted or unsubstituted phenyl, heteroaryl, or biaryl. The language "cyclic moiety" also includes non-aromatic cyclic moieties, such as, substituted or unsubstituted cyclic alkanes, (e.g.,
20 cyclohexane, and cyclopentane), cyclic alkenes (e.g., cyclohexene), and substituted or unsubstituted heterocycles (e.g., thiofuran, pyrimidine, pyrazine, pyrrole, imidazole, quinoxaline, etc.). The language "cyclic moiety" comprises not only the heterocyclic or carbocyclic moieties, but also may additionally include moieties which further comprise linking moieties, such as L₁ and L₂ which, for example, may link the anchor moiety to
25 the carbocyclic or heterocyclic cyclic portion of the cyclic moiety. Furthermore, linking moieties may also link the heterocyclic or carbocyclic cyclic moiety to the MC4-R interacting moiety. Examples of cyclic moieties include unsubstituted phenyl, halogenated phenyl (e.g., fluoro, bromo, chloro and iodo phenyl), alkyl substituted phenyl (e.g., methyl, ethyl, propyl, etc.), amino substituted phenyl, heteroaryls (e.g.,
30 thiofuran, pyridine, quinoxaline, pyrazine, pyrrole, etc.).

The language "MC4-R interacting moiety" ("E") includes moieties which permit the MC4-R binding compound to perform its intended function, e.g., interact with the MC4-R. Examples of MC4-R interacting moieties include substituted or unsubstituted alkyl (e.g., substituted with amino, cyano, nitro, hydroxy, etc.), aryl (e.g., phenyl,
35 heteroaryl), amino (e.g., 3-aminopropylamino, dimethyl amino, diethyl amino), amidino, guanidino, carbocyclic and heterocyclic moieties. The language "MC4-R interacting moiety" is not intended to suggest that this moiety is the active pharmacophore of the

molecule, responsible for the pharmacological, binding or other properties of the MC4-R binding compound.

In one embodiment, the MC4-R interacting moiety is cyclic, e.g., aryl, alkyl, biaryl, polycyclic, heteroaromatic, or heterocyclic. Examples of heterocyclic MC4-R interacting moieties include heterocycles which contain nitrogen atoms, such as, substituted and unsubstituted imidazolyl, imidazolyl, pyridinyl, pyrrolyl, piperazinyl, imidoazopyridinyl, pyrroloimidazolyl, pyrrolyl, azetidyl, azapanyl, pyrimidinyl, pyridinyl, morpholinyl, diazapanyl, and piperidinyl moieties. The MC4-R interacting moiety may be bicyclic, polycyclic, bridged or a fused ring system. Examples of fused and bridged heterocycles include:

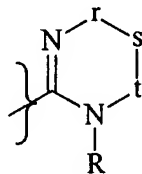


The substituent R includes substituted and unsubstituted alkyl (e.g., methyl, ethyl, etc.), arylcarbonyl, alkoxycarbonyl, alkylcarbonyl, arylalkylcarbonyl, and other groups which allow the MC4-R interacting moiety to perform its intended function.

The MC4-R interacting moiety can be substituted with substituents such as, but not limited to, halogens (e.g., fluorine, chlorine, bromine, iodine, etc.), alkyl (e.g., substituted or unsubstituted, branched straight chain or cyclic, e.g., methyl, ethyl, propyl, butyl, pentyl, etc.), alkenyl, alkynyl, hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy, carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonate, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, aminoalkyl, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, azido, heterocyclyl, alkylaryl, aryl, heteroaryl moieties and combinations thereof.

In another embodiment, the MC4-R interacting moiety is not cyclic, e.g., the MC4-R interacting moiety is alkyl, unsubstituted amino, alkylamino, dialkylamino, amidino, guanidino, etc. Examples of alkyl MC4-R interacting moieties include straight and branched chain alkyls such as n-butyl, n-pentyl, and n-hexyl.

In another embodiment, the MC4-R interacting moiety contains one or more nitrogen atoms, e.g., pyridinyl, pyrrolyl, pyrazinyl, imidazolyl, imidazolinyl, quinoxalinyl, or pyrimidinyl. In a further embodiment, the MC4-R interacting moiety is of the formula (XIII):



(XIII)

wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

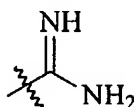
t is CH, CH₂, CHR³, CR³R⁴, or H;

s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;

R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to A, B, L₁, L₂, R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings;

R¹, R², R³, R⁴, R⁵, and R⁶ are each substituted or unsubstituted alkyl, alkenyl, alkynyl, heterocyclic, halogen, thiol, thioether, thioalkyl, hydroxyl, nitro, amino, cyano, or alkoxy, and may optionally be linked to form a carbocyclic or heterocyclic ring. The carbocyclic ring that is formed through the linkage of R, R¹, R², R³, R⁴, R⁵, or R⁶ may be bridged, fused, or spiro.

In one embodiment, the MC4-R interacting moiety is represented by the formula (XIV) below, when s is absent:



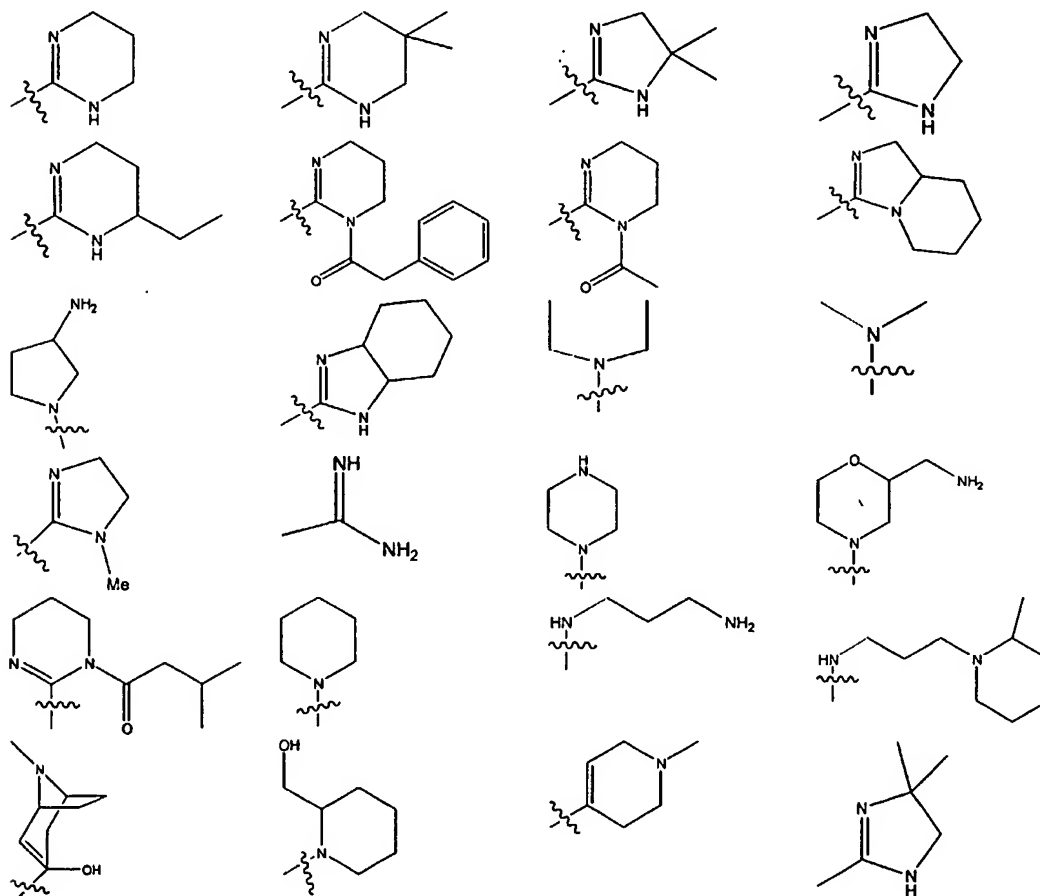
(XIV)

For example, in another further embodiment, the MC4-R interacting moiety may be bicyclic, e.g., biheterocyclic, for example, quinoxalinyl. The language "linked to form a ring" refers to moieties covalently connected through a chain of atoms (e.g., carbon atoms and/or heteroatoms). The chain of atoms can comprise any number of atoms, which allow the MC4-R binding moiety to perform its intended function. In a further embodiment, the chain of atoms is selected such that a ring with three, four, five, six, seven, or eight members are formed. The ring that can be formed may be spiro (e.g., connected through the same carbon atom), fused (connected through adjacent carbon atoms), or bridged (e.g., connected through carbon atoms which are neither identical nor adjacent). In an embodiment, R and t are linked, e.g., to form a bicyclic

moiety. Examples of bicyclic moieties include, but are not limited to, imidazopyridinyl, pyrroloimidazolyl, cyclopentaimidazolyl, pyridopyrimidinyl, etc.

- In a further embodiment R is H, alkyl, benzocarboxy, alkylcarboxy, or arylalkylcarboxy. In another further embodiment, s is CR^5R^6 and R^5 and R^6 are each methyl. In another further embodiment, r is a covalent bond, and at least one of t and s are CH_2 . In another, t, r, and s are each CH_2 . In another, r is a covalent bond, and t and s are linked through a 4 carbon chain. In another further embodiment, at least one R group is OH. In an embodiment, r is a covalent bond, t is CR^3R^4 , and s is CR^5R^6 , wherein R^3 , R^4 , R^5 and R^6 are each independently hydrogen or alkyl (e.g., methyl, ethyl, propyl, or butyl).

Examples of MC4-R interacting moieties include, but are not limited to, the following structures:



In another embodiment, the invention pertains to a method for treating an MC4-R associated state in a mammal, by administering an effective amount of a MC4-R binding compound to a mammal, such that the MC4-R associated state is treated. Examples of MC4-R binding compounds include compounds comprising the formula

5 (II):



wherein:

B is an anchor moiety;

A is a cyclic moiety; and

10 E is a MC4-R interacting moiety, and pharmaceutically acceptable salts thereof.

The MC4-R binding compounds of formula (II), may further comprise linking moieties, L_1 and L_2 . Such MC4-R binding compounds include compounds of the formula (III):

15



wherein B is an anchor moiety (as described above), L_1 and L_2 are linking moieties, A is a cyclic moiety (as described above), and E is a MC4-R interacting moiety. Pharmaceutically acceptable salts of the MC4-R binding compound are also included.

The language "linking moiety" includes moieties which link, preferably covalently, the MC4-R interacting moiety, the cyclic moiety, and the anchor moiety of the invention. Examples of linking moieties include covalent bonds, 1-10 atom chains which may be branched or unbranched, substituted or unsubstituted alkyl, heterocyclic, alkenyl, or alkynyl. The chains may be substituted with 0-3 heteroatoms or other moieties which allow the MC4-R binding compound to perform its intended function. Examples of suitable heteroatoms include sulfur, oxygen, nitrogen, and phosphorous. The invention contemplates MC4-R binding compounds which comprises more than

30 two linking moieties.

In an embodiment, L_1 is a chain of 1-10 atoms (e.g., such as carbon, nitrogen, oxygen, or sulfur atoms), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 atoms. In an embodiment, L_1 is selected from the group consisting of a covalent bond, C_1-C_6 , C_1-C_5 , C_1-C_4 , C_1-C_3 , C_1-C_2 , branched or unbranched alkyl, wherein one, two or three of the carbons are optionally replaced with any combination of substituted or unsubstituted oxygen, sulfur or nitrogen atoms. In a further embodiment, L_1 is a thioether (e.g., $-S-CH_2-$, $-S-CH(CH_3)-$, $-CH_2-S-CH_2-$, $-S-$, or $-S-CH-(C_6H_5)-$), an ether (e.g., $-O-CH_2$ or $-CH_2-O-CH_2-$), a sulfoxide, a sulfone, an amine (e.g., $-NH-$, $-NH-CH_2-$, $-NMe-CH_2-$, CH_2-NH-

CH₂-, etc.) or alkyl (e.g., -CH₂-CH₂-, -CH₂-, or -CH₂-CH₂-CH₂-). In another embodiment, L₁ comprises a sulfonyl group. Furthermore, L₁ can be substituted or unsubstituted (e.g., a hydrogen can be replaced by another moiety), such that the MC4-R binding compound is capable of performing its intended function, e.g., bind to or interact with the MC4-R. Examples of substituents include, but are not limited to, halogens (e.g., fluorine, chlorine, bromine, iodine, etc.), alkyl (e.g., substituted or unsubstituted, branched straight chain or cyclic, e.g., methyl, ethyl, propyl, butyl, pentyl, etc.), alkenyl, alkynyl, hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, azido, heterocyclyl, alkylaryl, aryl heteroaryl moieties, or combinations thereof.

In an embodiment, examples of L_2 include a covalent bond, a chain of 1-10 atoms (e.g., such as carbon, nitrogen, oxygen, or sulfur atoms), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 atoms. In an embodiment, L_1 is selected from the group consisting of a covalent bond, C_1-C_6 , C_1-C_5 , C_1-C_4 , C_1-C_3 , C_1-C_2 , branched or unbranched alkyl, wherein one, two or three of the carbons are optionally replaced with any combination of substituted or unsubstituted oxygen, sulfur or nitrogen atoms.. In a further embodiment, L_2 is a covalent bond, $-CH_2-$ or $-NH-$. Furthermore, L_2 may also comprise one or more carbonyl groups. For example, L_2 linkers include substituted urea groups ($NH-C=O-NH$), oxycarbonylamino groups ($-O-C=O-NH$), thiocarboynl groups, etc.

Furthermore, like L₁, L₂ can be substituted with any substituent such that the MC4-R binding compound is capable of performing its intended function. Examples of substituents include, but are not limited to, halogens (e.g., fluorine, chlorine, bromine, iodine, etc.), alkyl (e.g., substituted or unsubstituted, branched straight chain or cyclic, e.g., methyl, ethyl, propyl, butyl, pentyl, etc.), alkenyl, alkynyl, hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy, carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonate, phosphinate, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, azido, heterocyclyl, alkylaryl, aryl and heteroaryl moieties.

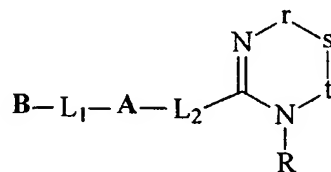
In a further embodiment, the MC4-R binding compound is of formula (III) (e.g., B-L₁-A-L₂-E), wherein B is substituted or unsubstituted biaryl (e.g., substituted or unsubstituted biphenyl, naphthyl, fluorenyl), unsubstituted or substituted heteroaryl (e.g., thienyl, benzothienyl, furanyl, pyrazinyl, pyrrolyl, pyrrolidinyl, etc.), unsubstituted or substituted phenyl, wherein one or more of said substituents are selected from the group consisting of halogens (e.g., bromine, fluorine, chlorine, iodine, etc.), alkyl groups (e.g., branched, straight chain or cyclic, substituted or unsubstituted, methyl, ethyl, propyl, butyl, etc.), alkoxy groups (e.g., substituted or unsubstituted alkoxy, e.g., methoxy, ethoxy, isopropoxy, n-propoxy, isobutoxy, n-butoxy, pentoxy, cyclopentoxy, methylenedioxy, ethylenedioxy, etc.), aryl groups (e.g., substituted or unsubstituted phenyl, heterocyclic groups), alkenyl, alkynyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, thiol, thioether, thioalkyl, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, and azido;

L₁ is a covalent bond, C₁-C₁₀ branched or unbranched alkyl, wherein one or more of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms;

A is a substituted or unsubstituted phenyl, heteroaryl (e.g., pyrrolyl, pyrazinyl, thienyl, pyridinyl, etc.), bicyclic (e.g., methylenedioxyphenyl, isoindole, indole, and indan) or biaryl (e.g., naphthyl, quinoxaliny, purinyl, etc.) wherein said substituent is selected from the group consisting of halogens (e.g., bromine, fluorine, chlorine, iodine, etc.), alkyl groups (e.g., branched, straight chain or cyclic, substituted or unsubstituted, methyl, ethyl, propyl, butyl, etc.), alkoxy groups (e.g., substituted or unsubstituted alkoxy, e.g., methoxy, ethoxy, isopropoxy, n-propoxy, isobutoxy, n-butoxy, pentoxy, cyclopentoxy, methylenedioxy, ethylenedioxy, etc.), aryl groups (e.g., substituted or unsubstituted phenyl, heterocyclic groups), alkenyl, alkynyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, and azido;

L₂ is a covalent bond, a chain of 1-10 atoms (e.g., such as carbon, nitrogen, oxygen, or sulfur atoms), e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 atoms. In an embodiment, L₁ is selected from the group consisting of a covalent bond, C₁-C₆, C₁-C₅, C₁-C₄, C₁-C₃, C₁-C₂, branched or unbranched alkyl, wherein one, two or three of the carbons are
 5 optionally replaced with oxygen, sulfur or nitrogen atoms, substituted or unsubstituted amino (e.g., -NH-, -NH-CH₂), ether, thioether, or alkyl (e.g., C₁-C₁₀, -CH₂-, -CH₂-CH₂-, or -CH₂-CH₂-CH₂-, etc.);

E is unsubstituted amino, unsubstituted and substituted alkylamino (e.g., 3-aminopropylamino), dialkylamino (e.g., dimethyl amino, diethyl amino), amidino,
 10 guanidino, heterocyclic (e.g., substituted and unsubstituted imidazolyl, imidazolyl, piprazinyl, morpholinyl, piperidinyl, imidoazopyridinyl, pyrroloimidazolyl, pyridinyl, or pyrimidinyl) moieties, aryl (e.g., phenyl, heteroaromatic, e.g., substituted and unsubstituted pyrazinyl, imidazolyl, quinoxalinyl, or pyrimidinyl), wherein said substituents include, but are not limited to, amino (e.g., unsubstituted amino,
 15 alkylamino, dialkyl amino), aminoalkyl (e.g., methylamino, ethylamino, propylamino, etc.), alkyl (e.g., branched and straight chain, substituted and unsubstituted (e.g., carboxy, hydroxy, halogen, amino, cyano, nitro, etc. substituted), methyl, ethyl, propyl, butyl, etc.), aryl (e.g., phenyl, heteroaromatic), alkenyl (e.g., branched or straight chain, substituted or unsubstituted), alkynyl, etc. and pharmaceutically acceptable salts thereof.
 20 In another embodiment, the invention pertains to a method for treating an MC4-R associated state in a mammal by administering an effective amount of a MC4-R binding compound to a mammal, such that the MC4-R associated state is treated. In an embodiment, the compound is of the formula (IV):



(IV)

25 wherein

A is a substituted or unsubstituted phenyl, heteroaryl (e.g., pyrrolyl, pyrazinyl, pyridinyl, etc.), or biaryl (e.g., naphthyl, quinoxalinyl, purinyl, etc.) wherein said substituent is selected from the group consisting of halogens (e.g., bromine, fluorine, chlorine, iodine, etc.), alkyl groups (e.g., branched, straight chain or cyclic, substituted
 30 or unsubstituted, methyl, ethyl, propyl, butyl, etc.), alkoxy groups (e.g., substituted or unsubstituted alkoxy, e.g., methoxy, ethoxy, isopropoxy, n-propoxy, isobutoxy, n-butoxy, pentoxy, cyclopentoxy, methylenedioxy, ethylenedioxy, etc.), aryl groups (e.g., substituted or unsubstituted phenyl, heterocyclic groups), alkenyl, alkynyl, hydroxyl,

alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including
 5 alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, and azido;

B is substituted or unsubstituted biaryl (e.g., substituted or unsubstituted biphenyl, naphthyl, fluorenyl), unsubstituted or substituted heteroaryl (e.g., thienyl,
 10 benzothienyl, furanyl, pyrazinyl, pyrrolyl, pyrrolidinyl, etc.), unsubstituted or substituted phenyl, wherein one or more of said substituents are selected from the group consisting of halogens (e.g., bromine, fluorine, chlorine, iodine, etc.), alkyl groups (e.g., branched, straight chain or cyclic, substituted or unsubstituted, methyl, ethyl, propyl, butyl, etc.), alkoxy groups (e.g., substituted or unsubstituted alkoxy, e.g., methoxy, ethoxy,
 15 isopropoxy, n-propoxy, isobutoxy, n-butoxy, pentoxy, cyclopentoxy, methylenedioxy, ethylenedioxy, etc.), aryl groups (e.g., substituted or unsubstituted phenyl, heterocyclic groups), alkenyl, alkynyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino
 20 (including alkyl amino, dialkylamino, thiol, thioether, thioalkyl, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, and azido;

L₁ and L₂ are selected from the group consisting of a covalent bond, C₁-
 25 C₄ branched or unbranched, substituted or unsubstituted alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms;

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

t is CH, CH₂, CHR³, CR³R⁴, or H;

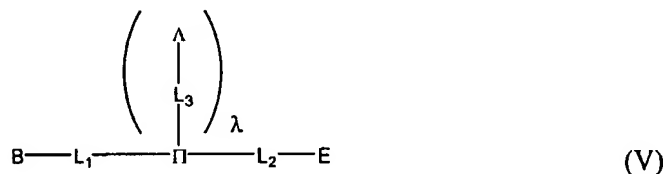
s is CHR₅, CR₅R₆ or absent (e.g., leaving a non-cyclic diamine);

30 R is H, substituted or unsubstituted alkyl, arylalkyl, or heteroalkyl, and may optionally be linked to A, B, L₁, or L₂;

R¹, R², R³, R⁴, R⁵, and R⁶ are each substituted or unsubstituted alkyl, halogen, thiol, thioether, thioalkyl, alkoxy, and may be optionally linked to each other to form additional ring moieties, e.g., quinoxalinyll. Pharmaceutically acceptable salts of
 35 the MC4-R binding compounds are also included.

In one further embodiment, A is substituted or unsubstituted phenyl. Examples of substituents include halogens (e.g., fluorine, chlorine, iodine, bromine), alkoxy, alkyl (e.g., methyl, trifluoromethyl), and amino moieties. In other embodiments, A is heteroaromatic, (e.g., thienyl), or biaryl, (e.g., naphthyl or quinoxaliny).

- 5 The invention also pertains to methods for treating an MC4-R associated state in a mammal comprising by administering an effective amount of a MC4-R binding compound of the formula (V):



- 10 B is substituted or unsubstituted biaryl, unsubstituted or substituted heterocyclic, or unsubstituted or substituted phenyl, wherein one or more of said substituents are halogens, alkyl, alkynyl, alkoxy, aryl, amino, thiol, thioether, thioalkyl, cyano, or nitro;

L₁ is a covalent bond, C₁-C₁₀ branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms;

- 15 L₂ is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl;

E is substituted or unsubstituted alkyl, amino, amidino, guanidino, heterocyclic, or aryl, wherein said substituents are amino, arylalkyl, aminoalkyl, alkyl, aryl, alkenyl, or alkynyl;

- 20 Π is a covalent bond, a carbon atom, a nitrogen atom, heterocyclic, alkyl, carbocyclic, or aryl;

L₃ is a covalent bond, C₁-C₆ branched, unbranched or cyclic alkyl (wherein one, two or three of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms), carbonyl, aminocarbonyl, aminocarbonylamino, aminocarbonyloxy, or an

- 25 aminothiocabonyl moiety; and

A is substituted or unsubstituted heterocyclic, aryl, alkoxy, amino, alkyl, alkenyl, alkynyl, or hydrogen; and

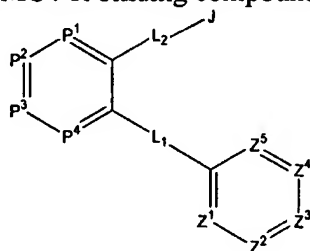
λ is 0, 1 or 2, and pharmaceutically acceptable salts thereof.

- Examples of MC4-R binding compounds with this structure include, but are not
 30 limited to, compounds, wherein Π is a carbon atom, L₃ is aminocarbonyloxy, A is substituted aryl, λ is one, L₁ and L₂ are each CH₂, and B and E are each pipridinyl. Examples of substituents for A include but are not limited to, alkoxy (e.g., C₁-C₁₀ alkoxy, e.g., methoxy, ethoxy, propoxy, butoxy, pentoxy, hexoxy, heptoxy, octoxy, nonoxy, and decoxy), cyano, halogens (e.g., fluorine, chlorine, bromine, iodine), alkyl (e.g., straight or branched chain, etc.), aryl, alkenyl, alkynyl, nitro, amino, or any other
 35

substituents which enables the MC4-R binding compound to perform its intended function, *e.g.*, treat an MC4-R associated state.

Other examples of compounds of formula (V) include, but are not limited to, compounds wherein Π , L_2 and L_3 together are a single covalent bond, E is alkyl, and B is substituted or unsubstituted heterocyclic. In other compounds of formula (V), Π is a nitrogen atom, L_2 , L_1 and L_3 are each alkyl, E is substituted amino (*e.g.*, alkyl substituted), or heterocyclic (*e.g.*, piperazinyl, piperidinyl, morpholinyl, etc.) and B and A are each aryl (*e.g.*, phenyl, anthracenyl, biaryl, *e.g.*, naphthyl).

In another further embodiment, the invention pertains to yet another method for treating an MC4-R associated state in a mammal by administering to a mammal an effective amount of a MC4-R binding compound of the formula(VI):



(VI)

wherein

- P^1 , P^2 , P^3 , and P^4 are optionally substituted carbon, sulfur, or nitrogen, and wherein one of P^1 , P^2 , P^3 , and P^4 may represent a covalent bond;
- Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 are optionally substituted carbon or nitrogen;
- L^1 is a covalent bond, C_1 - C_6 branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms;
- L_2 is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl;
- J is an unsubstituted or substituted nitrogen containing heterocycle or a substituted or unsubstituted amino group, and pharmaceutically acceptable salts thereof.
- Examples of substituents of P^1 , P^2 , P^3 , P^4 , Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 include halogens (*e.g.*, bromine, fluorine, chlorine, iodine, etc.), alkyl groups (*e.g.*, branched, straight chain or cyclic, substituted or unsubstituted, methyl, ethyl, propyl, butyl, etc.), alkoxy groups (*e.g.*, substituted or unsubstituted alkoxy, *e.g.*, methoxy, ethoxy, isopropoxy, n-propoxy, isobutoxy, n-butoxy, pentoxy, cyclopentoxy, methylenedioxy, ethylenedioxy, etc.), aryl groups (*e.g.*, substituted or unsubstituted phenyl, heterocyclic groups), alkenyl, alkynyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxy carbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonate, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino,

imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, and azido groups.

In a further embodiment, P^1 , P^2 , P^3 , and P^4 are each substituted or unsubstituted carbon (e.g., CH). For example, P^1 and P^3 may be CH. In another further embodiment, P^2 and P^4 are each CH, CF, CCl, CBr, Cl, C-aryl, C-alkyl (e.g., \dot{C} -Me, C-ethyl, C-propyl, etc.) C-alkoxy (e.g., C-OMe, C-O-ethyl, C-OCF₃, etc.). In a further embodiment, P^2 is CH and P^4 is CCl or CF. In an embodiment, P^1 is a covalent bond, P^2 and P^3 are each optionally substituted carbon, and P^4 is S (e.g., thienyl).

In a third further embodiment, Z^3 and Z^4 are each CH.

In a fourth further embodiment, Z^1 is CH, or covalently linked to Z^2 to form a naphthyl ring. Examples of Z^2 include CH, C-(C \equiv CH), CCl, CBr, Cl, and CF. Furthermore, Z^2 may be substituted with a chain of atoms which covalently links it to Z^1 to form a naphthyl ring.

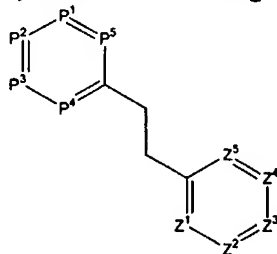
Examples of Z^5 include, but are not limited to, CH and C-alkoxy. The term "C-alkoxy" includes carbon atoms covalently bound to an alkoxy group, as described below. Examples of alkoxy groups include methoxy, ethoxy, propoxy, butoxy, etc.

In yet another further embodiment, L_2 is a covalent bond.

Examples of J include, but are not limited to, substituted or unsubstituted piperazinyl, imidoazopyridinyl, pyrroloimidazolyl, pyrrolyl, azetidiny, azapanyl, diazapanyl, pyrimidinyl, pyridinyl, morpholinyl, or piperidinyl. Furthermore, J may be a substituted or unsubstituted fused ring or bridged heterocycle.

In a further embodiment, each of P^1 , P^2 , P^3 , and P^4 are each optionally substituted carbon; Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 are each also optionally substituted carbon (e.g., alkoxy substituted, halogen substituted or linked to form a ring); wherein L_1 is either -S-CH₂-, or CH₂-CH₂. In a further embodiment, L_2 is a covalent bond and J is a moiety of formula XIII, as described above.

In another embodiment, the MC4-R binding compound is of formula (VII):



(VII)

wherein

Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 are CH, N, or substituted carbon; and P^1 , P^2 , P^3 , P^4 , and P^5 are CH, N or substituted carbon.

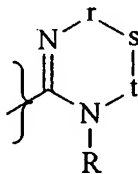
Examples of substituents of Z^1 , Z^2 , Z^3 , Z^4 , Z^5 , P^1 , P^2 , P^3 , P^4 , and P^5 include halogens (e.g., bromine, fluorine, chlorine, iodine, etc.), alkyl groups (e.g., branched, straight chain or cyclic, substituted or unsubstituted, methyl, ethyl, propyl, butyl, etc.), alkoxy groups (e.g., substituted or unsubstituted alkoxy, e.g., methoxy, ethoxy, isopropoxy, n-propoxy, isobutoxy, n-butoxy, pentoxy, cyclopentoxy, methylenedioxy, ethylenedioxy, etc.), aryl groups (e.g., substituted or unsubstituted phenyl, heterocyclic groups), alkenyl, alkynyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, and azido groups.

In a further embodiment, P^1 , P^2 , P^3 , P^4 and P^5 are each substituted or unsubstituted carbon (e.g., CH). For example, P^1 and P^3 may be CH. In another further embodiment, P^2 and P^4 are each CH, CF, CCl, CBr, or Cl. Furthermore, P^1 , P^2 , P^3 , and P^4 can be linked covalently to form a bicyclic ring.

In a third further embodiment, Z^3 and Z^4 are each CH.

In a fourth further embodiment, Z^1 is CH, or covalently linked to Z^2 to form a naphthyl ring. Examples of Z^2 include CH, C-(C \equiv CH), CCl, CBr, Cl, and CF. Furthermore, Z^2 may be substituted with a chain of atoms which covalently links it to Z^1 to form a naphthyl ring.

In a further embodiment, P^5 is C- L_2 -J, wherein C is a carbon atom, L_2 is a linking moiety, e.g., a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl; and J is an unsubstituted or substituted nitrogen containing heterocycle or a substituted or unsubstituted amino group. In yet a further embodiment, L_2 is a covalent bond and J is a moiety of formula (XIII):



(XIII)

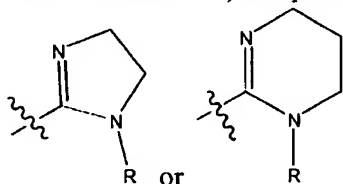
wherein

- 30 r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;
 t is CH, CH₂, CHR³, CR³R⁴, or H;
 s is CH, CH₂, alkenyl, CHR⁵, CR⁵R⁶, or absent;

R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxy carbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to A, B, L₁, L₂, R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and

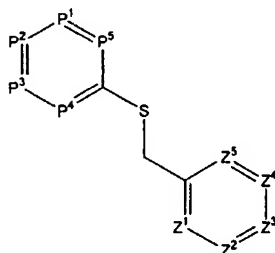
- R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioether, thioalkyl, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl, optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

In a further embodiment, compounds of formula VII also include compounds



- wherein J is or wherein R is alkyl (e.g., methyl, ethyl, propyl, butyl, etc.) or hydrogen. In another embodiment, the compounds include those in which P¹, P², and P³ are each CH, and P⁴ is CCl. Furthermore, the compounds also include those wherein Z¹, Z³, and Z⁴ are each CH, Z⁵ is COMe, and Z² is CBr, as well as those wherein Z¹ is covalently linked to Z² to form a naphthyl ring, and Z³, Z⁴ and Z⁵ are each CH.

- In another embodiment, the MC4-R binding compound is of formula (VIII):



(VIII)

wherein

- Z¹, Z², Z³, Z⁴, and Z⁵ are CH, N, or substituted carbon; and P¹, P², P³, P⁴, and P⁵ are CH, N or substituted carbon. Examples of substituents of Z¹, Z², Z³, Z⁴, Z⁵, P¹, P², P³, P⁴, and P⁵ include halogens (e.g., bromine, fluorine, chlorine, iodine, etc.), alkyl groups (e.g., branched, straight chain or cyclic, substituted or unsubstituted, methyl, ethyl, propyl, butyl, etc.), alkoxy groups (e.g., substituted or unsubstituted alkoxy, e.g., methoxy, ethoxy, isopropoxy, n-propoxy, isobutoxy, n-butoxy, pentoxy, cyclopentoxy, methylenedioxy, ethylenedioxy, etc.), aryl groups (e.g., substituted or unsubstituted phenyl, heterocyclic groups), alkenyl, alkynyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxy carbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonate, phosphinate, cyano, amino

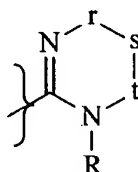
(including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, and azido groups.

5 In a further embodiment, P^1 , P^2 , P^3 , and P^4 are each substituted or unsubstituted carbon (e.g., CH). For example, P^1 and P^3 may be CH. In another further embodiment, P^2 and P^4 are each CH, CF, CCl, CBr, or Cl. Furthermore, P^1 , P^2 , P^3 , and P^4 can be linked covalently to form a bicyclic ring.

In a third further embodiment, Z^3 and Z^4 are each CH.

10 In a fourth further embodiment, Z^1 is CH, or covalently linked to Z^2 to form a naphthyl ring. Examples of Z^2 include CH, C-(C \equiv CH), CCl, CBr, Cl, and CF. Furthermore, Z^2 may be substituted with a chain of atoms which covalently links it to Z^1 to form a naphthyl ring.

In a further embodiment, P^5 is C- L_2 -J, wherein C is a carbon atom, L_2 is a linking moiety, e.g., a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl; and J is an unsubstituted or substituted nitrogen containing heterocycle or a substituted or unsubstituted amino group. In yet a further embodiment, L_2 is a covalent bond and J is a moiety of formula (XIII):



(XIII)

20 wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

t is CH, CH₂, CHR³, CR³R⁴, or H;

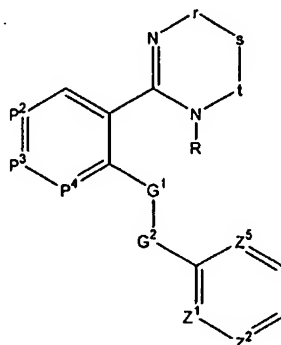
s is CH, CH₂, alkenyl, CHR⁵, CR⁵R⁶, or absent;

R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl, 25 arylalkylcarbonyl, alkylcarbonyl, optionally linked to A, B, L_1 , L_2 , R^1 , R^2 , R^3 , R^4 , R^5 , or R^6 to form one or more rings; and

R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are each halogen, thiol, thioether, thioalkyl, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, aryl, hydroxyl, nitro, amino, cyano, optionally linked to form a ring with R, R^1 , R^2 , R^3 , R^4 , R^5 , or R^6 .

30 In another embodiment, the invention pertains to MC4-R binding compounds of formulae VII and VIII. Examples of MC4-R binding compound of these formulae include, for example, compounds wherein P^5 is a carbon covalently bonded to a moiety of formula XIII. In a further embodiment, the moiety of formula XIII is not

benzoimidazole. In another further embodiment, Z^3 is not ethoxy. In another embodiment, the invention pertains to both methods of using and MC4-R binding compounds of formula (IX):



(IX)

5 wherein:

P^2 is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or a covalent bond;

P^3 is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, or Cl;

P^4 is CH, CCl, CBr, CF, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, or Cl;

10 G^1 and G^2 are each independently CH_2 , S, or O;

r is a covalent bond or CH_2 ;

t is CH_2 , CHR^3 , or CR^3R^4 ;

s is CH_2 , CHR^5 or CR^5R^6 ;

R is hydrogen alkyl, alkoxycarbonyl, or alkylcarbonyl;

15 Z^1 is CH, or covalently linked to Z^2 to form a naphthyl ring;

Z^2 is CH, C-($C\equiv CH$), CCl, CBr, Cl, CF, or covalently linked to Z^1 to form a naphthyl ring;

Z^5 is CH, C-alkoxy (e.g., C-OMe);

20 R^3 , R^4 , R^5 , and R^6 are methyl, ethyl, hydroxyl, alkoxy, halogen, cyano, nitro, amino, or pharmaceutically acceptable salts thereof.

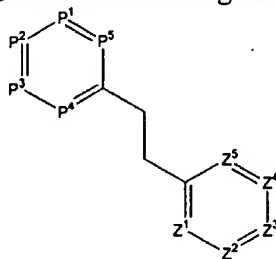
The language "linked to form a naphthyl ring" includes moieties which join Z^1 and Z^2 to form a naphthyl (fused) ring system. Examples of such Z^1 and Z^2 groups include, but are not limited to, $-CH=CH-CH=CH-$.

In a further embodiment, Z^1 is CH; Z^2 is CBr; and Z^5 is C-OMe.

25 In another further embodiment, P^2 is CH. In another, P^4 is CCl or CF. G^1 and G^2 are each CH_2 . In another, G^1 and G^2 together are $-CH_2-CH_2-$, $-CH_2-O-$, $-O-CH_2-$, $-CH_2-S-$ or $-S-CH_2-$. In another, Z^1 and Z^2 are linked to form a naphthyl ring.

In an embodiment, r is a covalent bond, s is CR^5R^6 , and t is CR^3R^4 , wherein R^3 , R^4 , R^5 , and R^6 are each independently hydrogen or alkyl (e.g., methyl, ethyl, propyl, or butyl). In another embodiment, R is hydrogen or alkyl (e.g., methyl, ethyl, propyl or butyl, etc.)

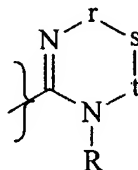
The invention pertains to MC4-R binding compound of the formula (VII):



(VII)

wherein

- 5 Z¹, Z², Z³, Z⁴, and Z⁵ are CH, N, or substituted carbon;
 P¹, P², P³, and P⁴ are CH, N or substituted carbon; and
 P⁵ is C-L₂-J, wherein L₂ is a covalent bond, alkyl (e.g., C₁-C₃), amino, ether, carbonyl, etc., and wherein J is a moiety of the formula (XIII):



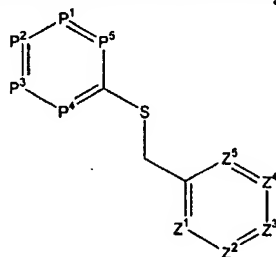
(XIII)

- 10 wherein

- r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;
 t is CH, CH₂, CHR³, CR³R⁴, or H;
 s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;
 R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl,
 15 arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and
 R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioether, thioalkyl, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl, optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

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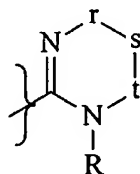
The invention also pertains to MC4-R binding compound of the formula (VIII):



(VIII)

wherein

Z^1, Z^2, Z^3, Z^4 , and Z^5 are CH, N, or substituted carbon;
 P^1, P^2, P^3 , and P^4 are CH, N or substituted carbon; and
 P^5 is C- L_2 -J, wherein L_2 is a covalent bond, alkyl (e.g., C₁-C₃), amino, ether, carbonyl, etc., and wherein J is a moiety of the formula (XIII):



5

(XIII)

wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

t is CH, CH₂, CHR³, CR³R⁴, or H;

s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;

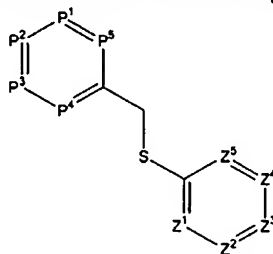
10

R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and

R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioalkyl, thioether, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl,

15 optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

The invention also pertains to MC4-R binding compound of the formula (XV):



(XV)

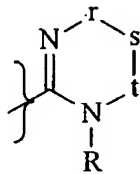
wherein

Z^1, Z^2, Z^3, Z^4 , and Z^5 are CH, N, or substituted carbon;

20

P^1, P^2, P^3 , and P^4 are CH, N or substituted carbon; and

P^5 is C- L_2 -J, wherein L_2 is a covalent bond, alkyl (e.g., C₁-C₃), amino, ether, carbonyl, etc., and wherein J is a moiety of the formula (XIII):



(XIII)

wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

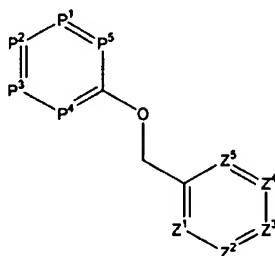
t is CH, CH₂, CHR³, CR³R⁴, or H;

s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;

5 R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and

10 R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioalkyl, thioether, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl, optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

The invention also pertains to MC4-R binding compound of the formula (XVI):



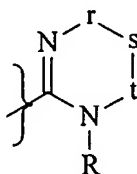
(XVI)

15 wherein

Z¹, Z², Z³, Z⁴, and Z⁵ are CH, N, or substituted carbon;

P¹, P², P³, and P⁴ are CH, N or substituted carbon; and

P⁵ is C-L₂-J, wherein L₂ is a covalent bond, alkyl (e.g., C₁-C₃), amino, ether, carbonyl, etc., and wherein J is a moiety of the formula (XIII):



(XIII)

wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

t is CH, CH₂, CHR³, CR³R⁴, or H;

s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;

25 R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and

R^1 , R^2 , R^3 , R^4 , R^5 , and R^6 are each halogen, thiol, thioether, thioalkyl, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl, optionally linked to form a ring with R , R^1 , R^2 , R^3 , R^4 , R^5 , or R^6 .

In a further embodiment, the invention includes compounds wherein P^1 , P^2 , P^3 ,
5 and P^4 of any one of formulas VII, VIII, XV, or XVI are each substituted or unsubstituted carbon. For example, in one embodiment, P^1 is CH. In another example, at least one of P^2 , P^3 and P^4 is a substituted carbon. In a further embodiment, P^2 , P^3 and P^4 are selected from the group consisting of CH, CF, Cl, CBr, C-alkyl, C-alkoxy, or Cl.

In another embodiment, the compounds of formulae VII, VIII, XV, or XVI,
10 include compounds wherein Z^3 and Z^4 are each CH. In another further embodiment of the formulae, Z^1 is CH. For example, in another further embodiment, Z^1 is covalently linked to Z^2 to form a naphthyl ring. Z^2 is CH, C-(C \equiv CH), CCl, CBr, Cl, and CF.

In another further embodiment, the compounds of the invention include compounds of formulae VII, VIII, XV, or XVI, wherein L_2 is a covalent bond. Also
15 included are compounds wherein R is H, alkyl, benzocarboxy, alkylcarboxy, or arylalkylcarboxy.

In another further embodiment, the compounds of the invention include compounds of formulae VII, VIII, XV, or XVI, wherein s is CR^5R^6 and R^5 and R^6 are each methyl. In another example r is a covalent bond. Alternatively, each of t , r and s
20 may be CH_2 .

In one further embodiment, the MC4-R binding compounds of the invention of formula VII do not include benzoimidazole as the moiety of formula XIII, when P^1 , P^2 , P^3 , P^4 , Z^1 , Z^2 , Z^4 , Z^3 , and Z^5 are each CH. Furthermore, in another further embodiment, the compounds of the invention do not include compounds wherein the moiety of
25 formula XIII is tetrahydropyrimidine, when P^1 , P^2 , P^3 , P^4 , Z^1 , Z^2 , Z^4 , and Z^5 are each CH and Z^3 is C-OEt or CH.

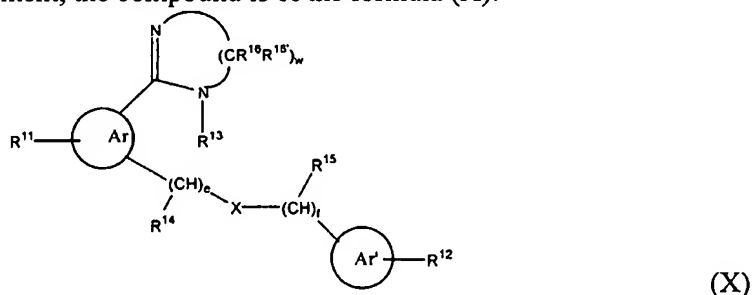
In another further embodiment, the MC4-R binding compounds of the invention of formula VIII, do not include compounds wherein the moiety of formula XIII is benzoimidazolyl. In another further embodiment, the MC4-R binding compounds of the invention of formula VIII, do not include compounds wherein P^2 is not Cl, if P^1 , P^3 , or P^4 are CH. In another further embodiment, the MC4-R binding compounds of the invention of formula VIII, do not include compounds wherein P^1 , P^2 , P^3 , P^4 , Z^1 , Z^2 , Z^4 , Z^3 , and Z^5 are each CH, when the moiety of formula XIII is tetrahydropyrimidine. In another further embodiment, the compounds of formula VIII of the invention do not
30 include compounds wherein the moiety of formula is 4,5-dihydro-1H-imidazole, when P^1 , P^2 , P^3 , and P^4 are each CH, and wherein one or two of Z^1 , Z^2 , or Z^3 is CCl, and the remaining Z groups are CH. In another further embodiments, the MC4-R binding compounds of formula VIII of the invention, do not include compounds wherein the
35

moiety of formula XIII is tetrahydropyrimidine, and when P^1 , P^2 , P^3 , and P^4 are each CH, and Z^2 is CCl and the remaining Z groups are CH. In another further embodiments, the compounds of formula VIII of the invention, do not include compounds wherein when the moiety of formula XIII is tetrahydropyrimidine, and when P^1 , P^2 , P^3 , and P^4 are each CH, and Z^1 and one of Z^4 or Z^5 are CCl and the remaining Z groups are CH.

In another further embodiment, the MC4-R binding compounds of the invention do not include compounds of formula XV, wherein the moiety of formula VIII is not benzoimidazole if P^1 , P^2 , P^3 , P^4 are each CH, and wherein Z^2 is CMe and the remaining Z groups are CH.

In another further embodiment, the MC4-R binding compounds of the invention do not include compounds of formula XVI, wherein the moiety of formula XVI, wherein L_2 is not NH (e.g., amino), if P^1 , P^2 , P^3 , P^4 , Z^1 , Z^2 , Z^4 , Z^3 , and Z^5 are each CH. In another embodiment, the MC4-R binding compounds of formula XVI of the invention do not include compounds wherein P groups are substituted to form a naphthyl ring.

In another embodiment, the invention features a method for treating an MC4-R associated state in a mammal by administering an effective amount of a MC4-R binding compound to a mammal. Compounds of formula (X) are also included in the invention. In this embodiment, the compound is of the formula (X):



wherein

Ar and Ar' are aromatic groups;

R^{11} is selected independently for each position capable of substitution from the group hydrogen, cyano, nitro, alkoxy, halogen, alkyl, amino, or aryloxy.

R^{12} is selected for each position capable of substitution from the group consisting of hydrogen, halogen, alkoxy, acetylenic, nitro, aryl, alkyl, alkenyl, alkynyl, cyano, acyl, or carbonyl;

R^{13} is hydrogen, alkenyl, alkynyl, aralkyl, nitro, cyano, alkyl (e.g., C_1 - C_{10} alkyl, e.g., methyl, ethyl, etc.) acyl, carbonyl, or SO_2CH_3 , and may optionally be linked to an R^{16} or an $R^{16'}$ group;

R^{16} and $R^{16'}$ are each independently selected for each position capable of substitution from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, heterocyclic, carbonyl, or acyl, and may optionally be connected through an alkyl chain to R^{13} or another R^{16} or $R^{16'}$ group, to form a fused or spiro ring system;

5 X is NR^{17} , S, O or a covalent bond;

R^{17} is hydrogen, alkyl, alkenyl, alkynyl, acyl, heterocyclic, or carbonyl;

R^{14} and R^{15} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, heteroaromatic, halogen, nitro, cyano, amino, or aryl, for each occurrence;

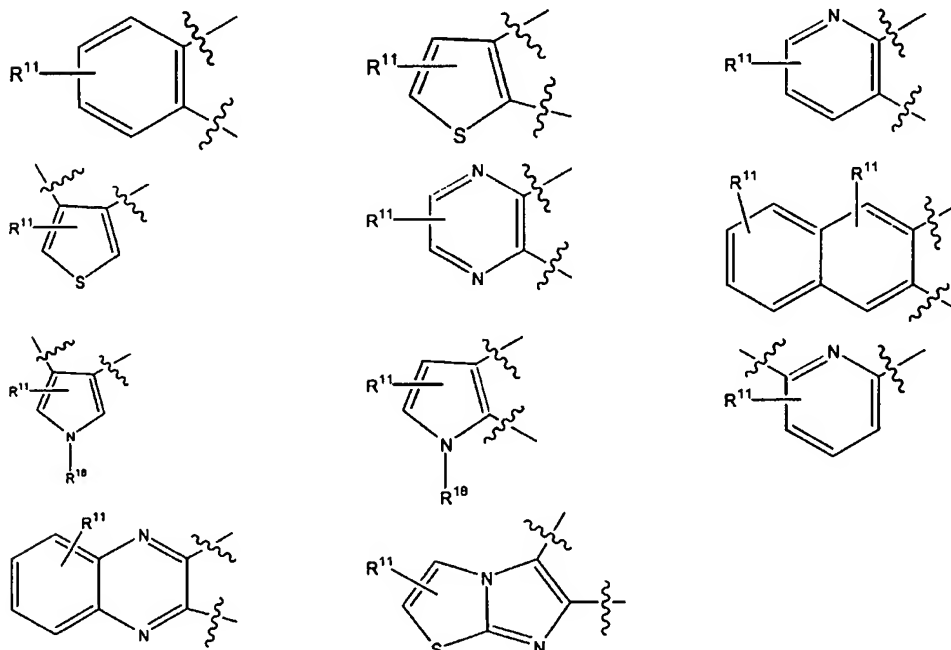
10 w is 0, 1, 2, 3, or 4;

e is 0, 1, 2, or 3;

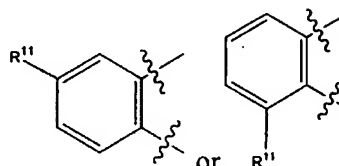
f is 0, 1, 2, or 3, and pharmaceutically acceptable salts thereof.

Examples of Ar groups include:

15



wherein R^{18} is acyl, alkyl or hydrogen.

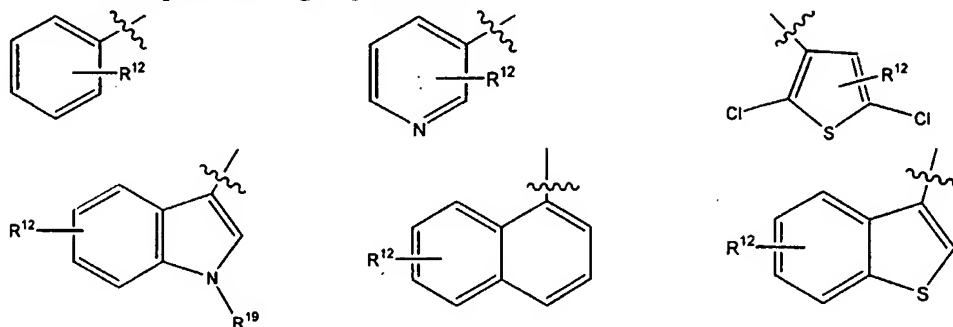


In a further embodiment, Ar is,

R^{11} is selected independently for each aromatic position capable of substitution. Exemplary R^{11} groups include, but are not limited to, hydrogen, halogen (e.g., fluorine, chlorine, or bromine), alkyl, amino, and benzyloxy.

20

Examples of Ar' groups include:



wherein R¹⁹ is hydrogen, alkyl, acyl, aryl, alkenyl, or alkynyl.

In a further embodiment, each R¹² group is selected independently from the group consisting of hydrogen, alkoxy, halogen (*e.g.*, fluorine, bromine, chlorine, or iodine), and cyano. Examples of alkoxy groups include C₁-C₁₀ alkoxy, such as, methoxy, ethoxy, n-propoxy, i-propoxy, and cyclopentoxy.

Examples of X include covalent bond, S, O and NR¹⁷. Examples of R¹⁷ include hydrogen, alkyl (*e.g.*, C₁-C₁₀ alkyl, *e.g.*, methyl), or acyl.

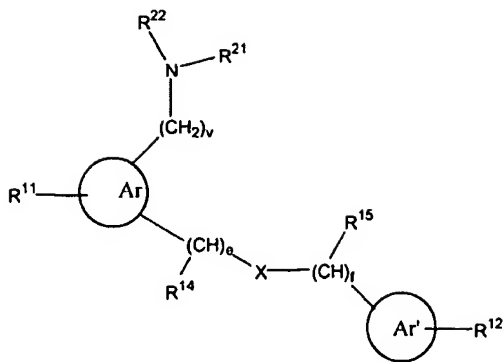
Examples of R¹⁶ and R^{16'} include alkyl and hydrogen. Each R¹⁶ and R^{16'} group is selected independently for each occurrence. In a further embodiment, at least one of R¹⁶ or R^{16'} are at least once hydrogen. In another embodiment, at least one of R¹⁶ or R^{16'} are at least once C₁-C₁₀ alkyl, *e.g.*, methyl or ethyl.

In yet another further embodiment, R¹⁴ and R¹⁵ are each independently hydrogen, alkyl (*e.g.*, C₁-C₁₀, *e.g.*, methyl) or phenyl for each occurrence.

In yet another further embodiment, R¹³ is hydrogen, acyl, alkyl (*e.g.*, C₁-C₁₀ alkyl, *e.g.*, methyl, ethyl, etc.) acyl, carboxy, or SO₂CH₃. Examples of acyl group include, but are not limited to, optionally substituted C₁-C₁₀alkyl acyl (*e.g.*, i-propylcarbonyl and benzylcarbonyl).

In yet another further embodiment, w is 2 or 3. In yet another further embodiment, e is 0 or 1. In yet another further embodiment, f is 0 or 1.

In another embodiment, the invention features a method for treating an MC4-R associated state in a mammal by administering an effective amount of a MC4-R binding compound to a mammal. In this embodiment, the compound is of the formula (XI):



(XI)

wherein

Ar and Ar' are aromatic groups, as described above;

R¹¹ is selected independently for each position capable of substitution
 5 from the group hydrogen, halogen, alkyl, amino, cyano, or aryloxy.

R¹² is selected for each position capable of substitution from the group
 consisting of hydrogen, halogen, alkoxy, acetylenic, nitro, aryl, alkyl, alkenyl, alkynyl,
 cyano, acyl, or carbonyl;

X is NR¹⁷, S, O or a covalent bond;

10 R¹⁷ is hydrogen, alkyl, acyl, heterocyclic, or carbonyl;

R¹⁴ and R¹⁵ are each independently selected from the group consisting of
 hydrogen, alkyl, alkenyl, or aryl, for each occurrence;

R²⁰ and R²¹ are each independently selected from the group consisting of
 substituted or unsubstituted alkyl, alkenyl, alkynyl, aryl, hydrogen, or carbonyl, and may
 15 optionally be linked to form a heterocycle (e.g., morpholinyl, piperazinyl, piperidinyl,
 etc.);

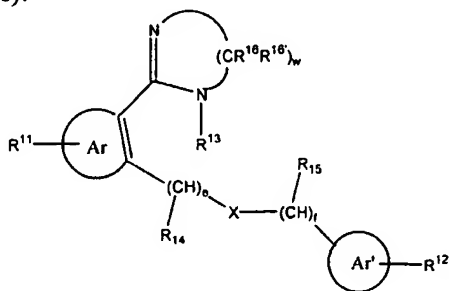
v is 0, 1, 2, 3, 4, 5, or 6;

e is 0, 1, 2, or 3;

f is 0, 1, 2, or 3, and pharmaceutically acceptable salts thereof.

20 Examples of Ar, Ar', R¹¹, R¹², R¹⁴, R¹⁵ and X moieties include those described
 for formula (X).

Other examples of MC4-R binding compounds include compounds of the
 formula (XVIII):



(XVIII)

wherein

Ar and Ar' are aromatic groups;

R¹¹ is selected independently for each position capable of substitution from the group hydrogen, cyano, alkoxy, nitro, halogen, alkyl, amino, or aryloxy;

5 R¹² is selected for each position capable of substitution from the group consisting of hydrogen, halogen, alkoxy, acetylenic, nitro, aryl, alkyl, alkenyl, alkynyl, cyano, acyl, or carbonyl;

R¹³ is hydrogen, alkenyl, alkynyl, aralkyl, nitro, cyano, alkyl, acyl, carbonyl, or SO₂CH₃, and may optionally be linked to an R¹⁶ or an R^{16'} group;

10 R¹⁶ and R^{16'} are each independently selected for each position capable of substitution from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, hydroxyl, cyano, aryl, heterocyclic, carbonyl, or acyl, and may optionally be connected through an alkyl chain to R¹³ or another R¹⁶ or R^{16'} group, to form a fused or spiro ring system;

X is NR¹⁷, S, O or a covalent bond;

15 R¹⁷ is hydrogen, alkyl, or carbonyl;

R¹⁴ and R¹⁵ are each independently hydrogen, halogen, or alkyl;

w is 1, 2, 3, or 4;

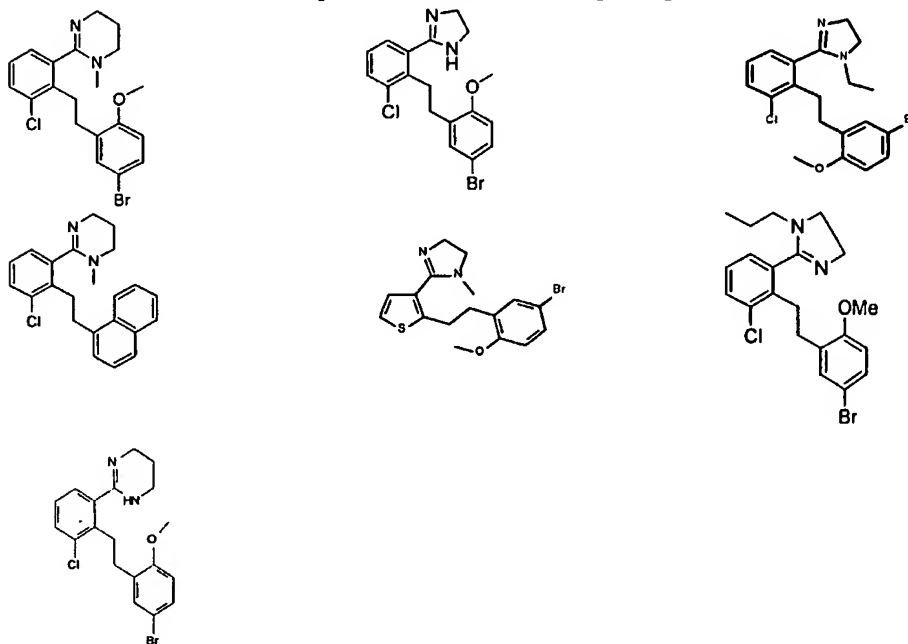
e is 0 or 1;

f is 0 or 1, wherein both e and f are not both 0 if X is a covalent bond,

20 and pharmaceutically acceptable salts thereof.

Examples of Ar, Ar', R¹¹, R¹², R¹⁴, R¹⁵, R¹⁶ and R^{16'} and X moieties include those described for formula (X).

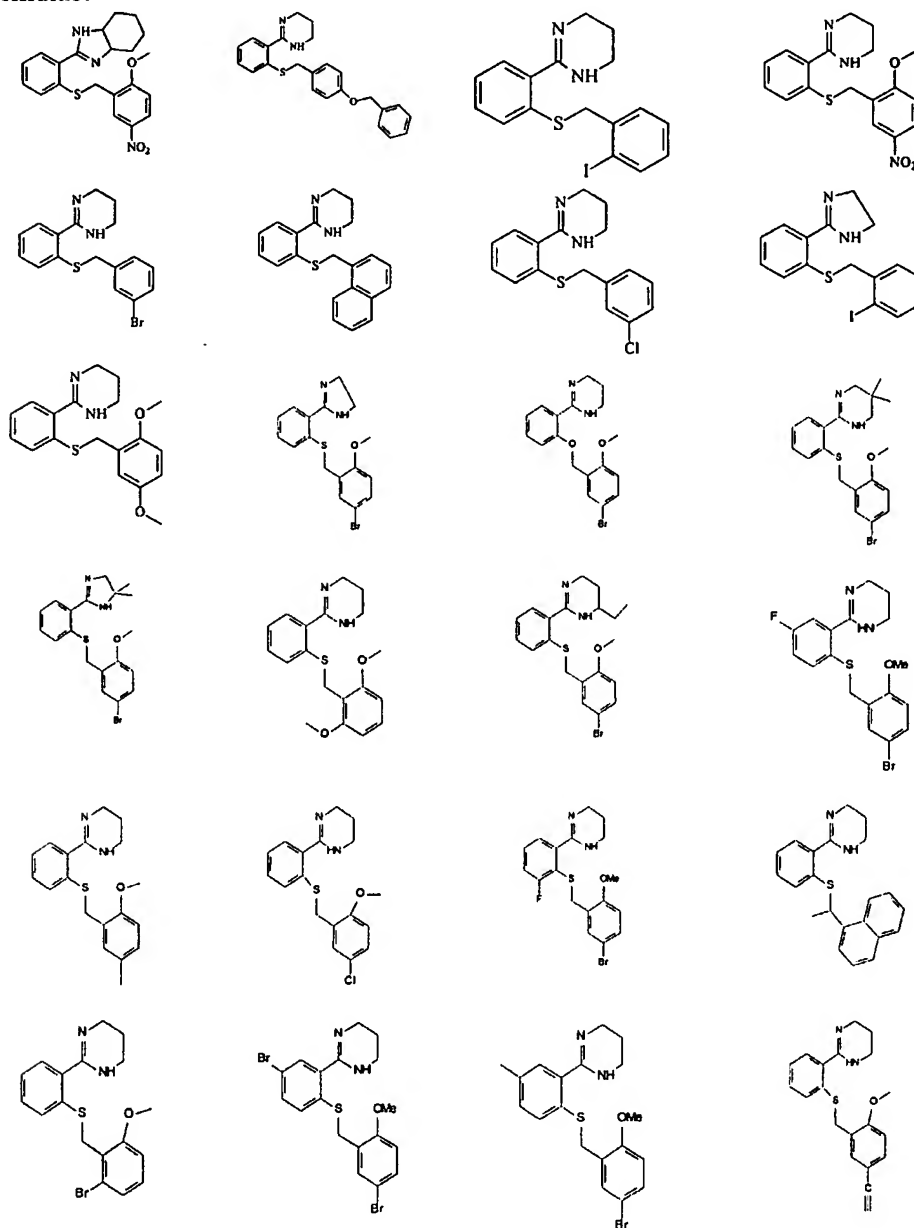
The invention also pertains to the following compounds:

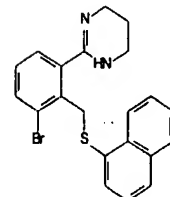
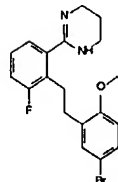
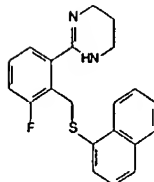
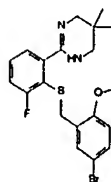
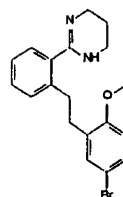
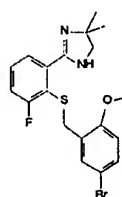
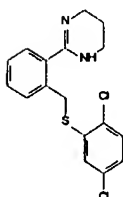
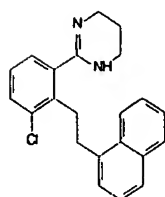
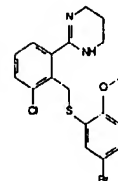
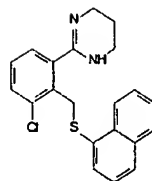
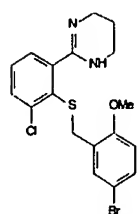
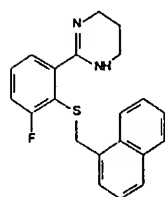
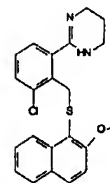
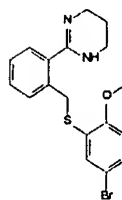
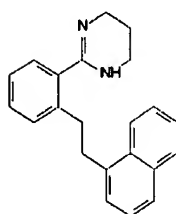
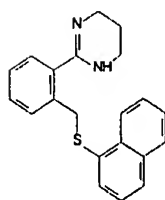
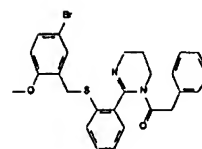
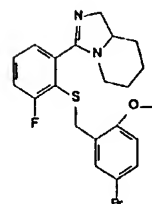
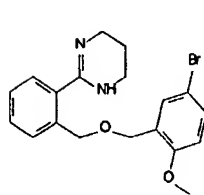
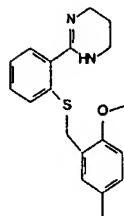
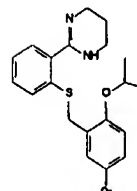
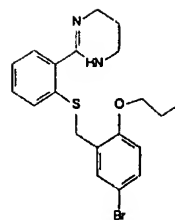
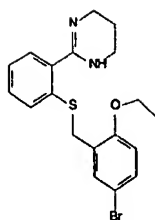
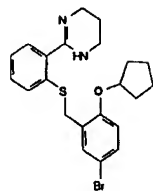


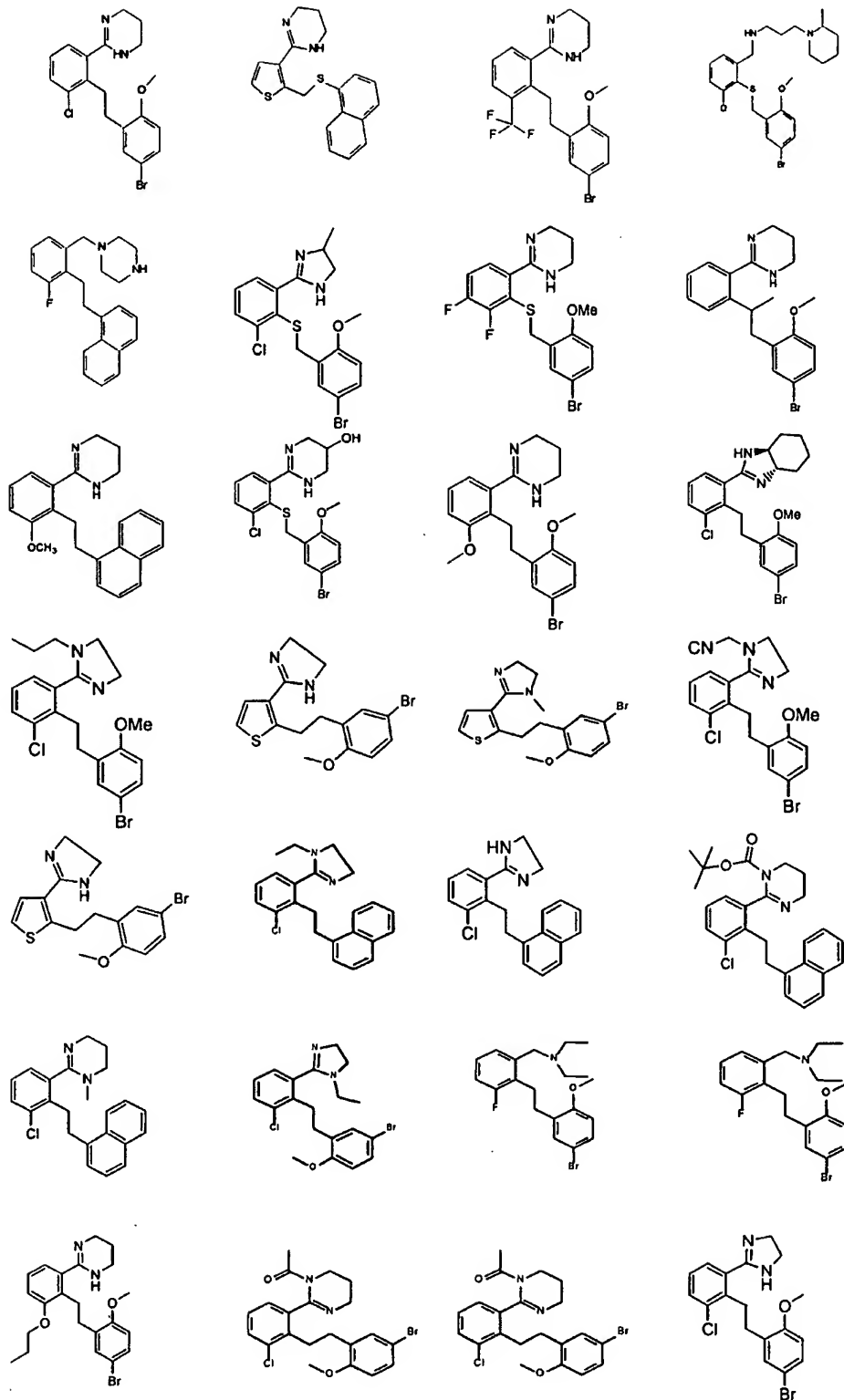
The invention also pertains to methods of using these compounds in methods for treating MC4-R associated states in a mammal by administering an effective amount of the compound to a mammal, such that the MC4-R associated state is treated, as well as pharmaceutical compositions comprising these compounds.

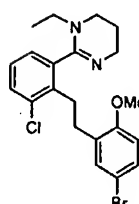
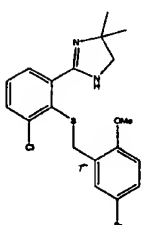
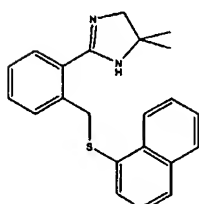
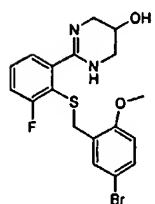
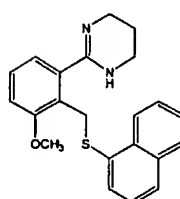
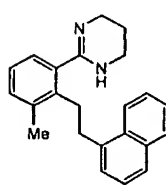
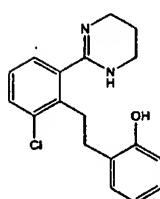
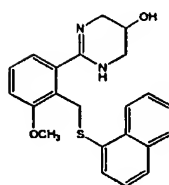
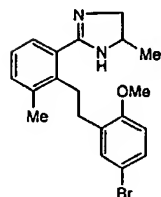
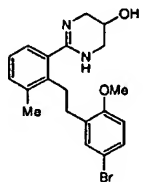
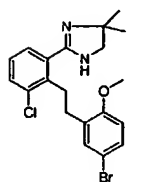
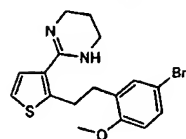
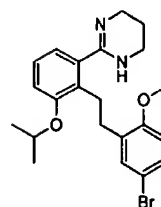
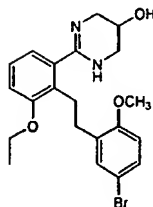
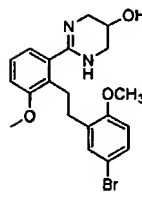
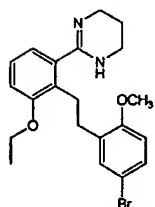
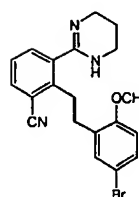
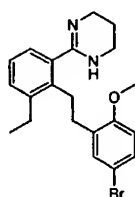
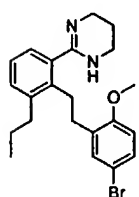
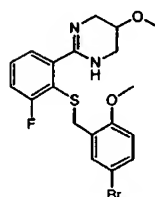
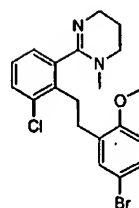
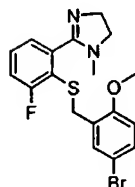
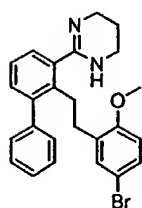
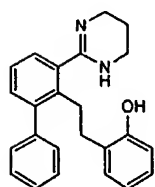
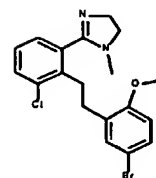
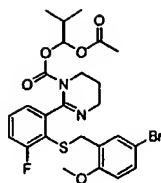
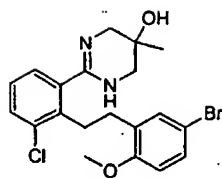
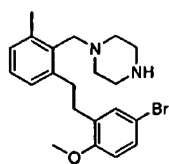
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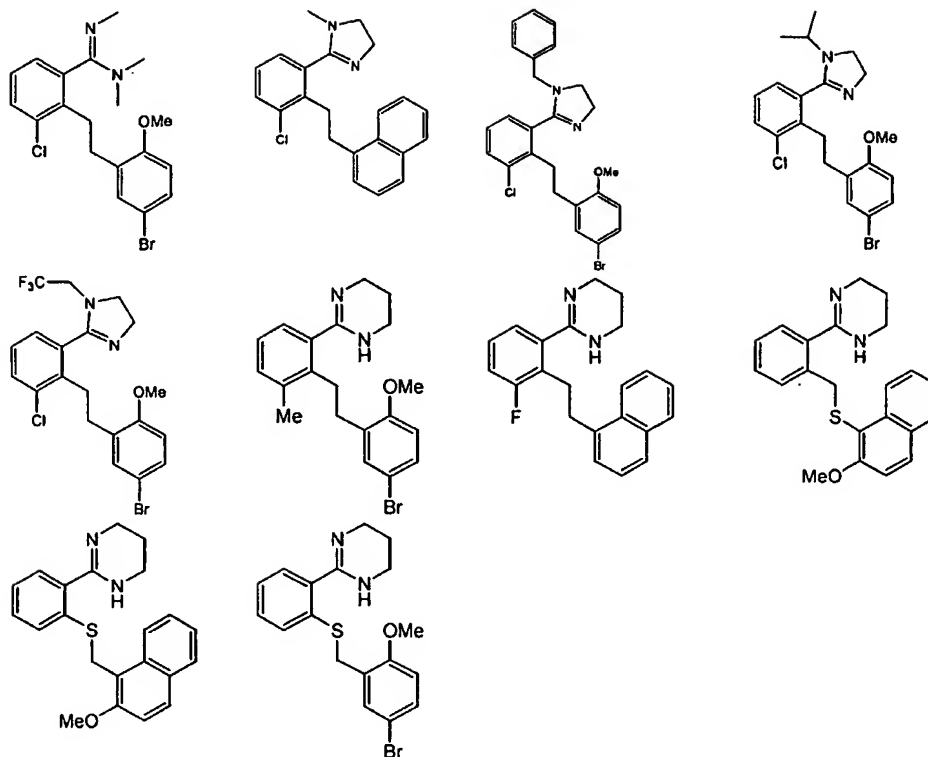
Other examples of MC4-R binding compounds include compounds of the formulae:











and pharmaceutically acceptable salts thereof.

The invention also includes MC4-R binding compounds such as:

- 2-[2-(4-benzyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2,5-dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[2-(3-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(3-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
- 2-[2-[2-(2-methoxy-naphthalen-1-yl)-ethyl]-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-[2-(2-methyl-naphthalen-1-yl)-ethyl]-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(2-(2,3-dihydro-benzo[1,4]dioxin-5-yl)-ethyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
- 2-[2-(2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
- 2-(2-Benzylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-(2-Pentadecylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 2-(2-Cyclohexylmethylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-Nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3,5-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[2-(4-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2,4-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(3,5-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-(2-Benzylsulfanyl-phenyl)-4,5-dihydro-1H-imidazole;
- 2-[2-(2,6-Difluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-(Naphthalen-1-ylmethoxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 1-{2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-ethanone;
- 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-
- 25 benzoimidazole;
- 2-[2-(2-Iodo-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
- 2-[2-(2,5-Dimethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 4-[2-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-quinoline;
- 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-pyridin-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 30 2-[2-(2-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Cyclopentylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(6-Methoxy-2,3-dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-
- 35 tetrahydro-pyrimidine;
- 2-[2-(5-fluoro-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 1-Methyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;

- 2-[2-(5-Bromo-2-methoxy-benzyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(Naphthalen-1-yloxymethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
5 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
2-[2-(2,6-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2-Bromo-6-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
10 2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[4-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2-Bromo-5-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
15 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(Biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Chloro-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2-Methoxy-5-thiophen-3-yl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
20 2-[2-(Biphenyl-2-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Iodo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(4,4'-Dimethoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(9H-Fluoren-9-ylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
30 2-[2-(3'-Chloro-4'-fluoro-4-methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(1-Naphthalen-1-yl-ethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-4,5-dihydro-1H-imidazole;
2-(2-Benzhydrylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
35 2-[2-(2'-Fluoro-4"-methoxy-[1,1';4',1"]terphenyl-3"-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzamidine;
2-[4-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(5-Ethynyl-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-cyclopentyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(5-Bromo-2-ethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-propoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperazine;
 C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-morpholin-2-yl}-
- 10 methylamine;
 2-[2-(2-Methoxy-5-methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylloxymethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-dimethyl-amine;
 2-[2-(5-Bromo-2-isopropoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(2-Ethoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Propoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-benzonitrile;
 1-{4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-phenyl}-
- 20 ethanone;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;
 C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-methylamine;
- 25 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,5,6,7,8,8a-hexahydro-imidazo[1,5-a]pyridine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole;
- 30 2-[2-(Benzo[b]thiophen-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Fluoro-2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-(Naphthalen-1-ylmethylsulfanyl)-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 35 2-[2-(2-Methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-3-methyl-butan-1-one;

- 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-
2-phenyl-ethanone;
2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyridin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
N-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-guanidine;
5 2-[2-(2-Isopropoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
2-[2-(2-Cyclopentyloxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
(5-Bromo-2-methoxy-benzyl)-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine;
10 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
2-[2-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
15 2-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(6-Bromo-2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
2-[3-Chloro-2-(2-methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
20 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-
pyrimidine;
2-[1-(2-Naphthalen-1-yl-ethyl)-1H-pyrrol-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
25 (5-Bromo-2-methoxy-benzyl)-methyl-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-
amine;
2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamine;
2-[2-(2-Chloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2-Bromo-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
30 2-(2-o-Tolylsulfanylmethyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2,5-Dichloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-(3-Amino-propylamino)-6-(5-bromo-2-methoxy-benzylsulfanyl)-benzonitrile;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;
[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
35 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-morpholine;
3'-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl;
2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-piperazin-1-yl-6,7-dihydro-quinoline;
1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;

- C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-methylamine;
- 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-pyrrolidin-3-ylamine;
- 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-pyrrolidin-3-ylamine;
- 5 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
- C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-morpholin-3-yl}-methylamine;
- 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-azetidine;
- 10 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ol;
- [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester;
- [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester;
- 15 [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester;
- {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-2-yl}-methanol;
- 4-tert-Butyl-N-naphthalen-1-ylmethyl-N-(2-piperidin-1-yl-ethyl)-benzamide;
- 20 N,N-Dimethyl-N'-naphthalen-2-ylmethyl-N'-naphthalen-1-ylmethyl-propane-1,3-diamine;
- N-(5-Bromo-2-methoxy-benzyl)-N',N'-dimethyl-N-naphthalen-1-ylmethyl-propane-1,3-diamine;
- 1-Naphthalen-1-ylmethyl-3-phenethyl-1-(2-piperidin-1-yl-ethyl)-thiourea;
- 25 3-(4-Dimethylamino-phenyl)-1-(3-dimethylamino-propyl)-1-naphthalen-1-ylmethyl-thiourea;
- 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzylamino]-piperidine-1-carboxylic acid ethyl ester;
- 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethylamine;
- 30 Naphthalene-2-sulfonic acid (2-dimethylamino-ethyl)-naphthalen-1-ylmethyl-amide;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-2-methoxymethyl-pyrrolidine;
- (2-Hexyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester;
- 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-pyrrolidine;
- 35 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-piperidine;
- 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-propan-1-ol;
- 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-3-methyl-butan-1-ol;

- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ol;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-2-yl}-methanol;
 {1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-ethyl-N-pyrrolidine;
 5 N-pyrrolyl-[1-(2-naphthalen-1-yl-ethyl)-pyrrolidin-2-ylmethyl]-amine;
 1-(2-Naphthalen-1-yl-ethyl)-piperidine-2-carboxylic acid methyl ester;
 (3-Bromo-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-amine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-piperidine;
 (5-Bromo-2-methoxy-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-
 10 amine;
 (1-Ethyl-pyrrolidin-2-ylmethyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
 (3-Bromo-benzyl)-(3-imidazol-1-yl-propyl)-naphthalen-1-ylmethyl-amine;
 (3-Imidazol-1-yl-propyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;
 15 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-1-piperidin-
 1-ylmethyl-ethyl ester;
 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-dimethylamino-ethyl ester;
 1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-
 20 amine;
 1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 N,N-Dimethyl-N'-(2-naphthalen-1-yl-ethyl)-N'-naphthalen-1-ylmethyl-ethane-1,2-
 diamine;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 25 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 {1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 30 {1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperidin-2-yl}-methanol;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-pyrrolidin-3-ylamine;
 1-Phenyl-3-piperazin-1-yl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-
 35 pyrimidine;
 2-[2-(4-Methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-phenylethynyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 pyrimidine;

- 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,5-Dimethoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 5 2-[2-(4-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
 10 2-[3-(Naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 15 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Bromo-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 20 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[4-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
 25 2-[2-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-trifluoromethyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Naphthalen-1-yl-ethyl)-3-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(6-Fluoro-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 30 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidin-2-yl}-methanol;
 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-[3-(2-methyl-piperidin-1-yl)-propyl]-amine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ylamine;
 35 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperazine;
 5,5-Dimethyl-2-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 5 3-(2-Naphthalen-1-yl-ethyl)-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
Amino-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-acetonitrile;
1-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethane-1,2-diamine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 10 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-1-methyl-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-(5-Bromo-2-methoxy benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
2-[2-(5-Bromo-2-methoxy-benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
2-[3-Methoxy-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-chloro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
- 30 2-[2-(1-Methyl-2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
3-(5-Bromo-2-methoxy-benzylsulfanyl)-2-fluoro-4-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 35 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;

- 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-fluoro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
- 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-Chloro-6-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-ethyl}-phenol;
- 10 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-5-methyl-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 15 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,4-dimethyl-4,5-dihydro-1H-imidazole;
- 20 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-4-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 4,4-Dimethyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-4,5-dihydro-oxazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-4-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 25 2-[5-(5-Bromo-2-methoxy-benzyl)-2-methyl-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 30 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 35 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 5 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-benzonitrile;
- 2-{3-Benzyloxy-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-butyl-phenyl}-1,4,5,6-tetrahydro-
- 10 pyrimidine;
- 2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-8-chloro-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-
- 20 pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isobutoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5-methoxy-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-
- 30 imidazole;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
- 2-{2-[3-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-biphenyl-2-yl]-ethyl}-phenol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-4,5-dihydro-
- 35 1H-imidazole;
- N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methoxy-benzamide;
- N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzamide;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-2-methyl-propyl ester;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 5 3-(5-Bromo-2-methoxy-phenyl)-5-chloro-3,4-dihydro-isoquinolin-1-ylamine;
 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(4-methoxy-benzoyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5-methyl-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 10 2-[(5-Bromo-2-methoxy-phenyl)-(3-piperidin-1-yl-propylamino)-methyl]-3-chloro-6-methyl-phenol;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperidine;
- 15 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-diethyl-amine;
 3-(5-Bromo-2-methoxy-phenyl)-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
- 20 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-methanol;
- 25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
- 30 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 35 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;

- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidin-2-yl)-
 methanol;
 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-
 5 benzamide;
 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
 10 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-
 imidazole;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-
 methanol;
 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-
 pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
 20 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-
 pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
 25 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-
 pyrimidin-1-yl)-ethanone;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
 30 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-
 benzamide;
 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-4,5-dihydro-1H-
 imidazole;
 35 {2-[3-(5-Bromo-2-methoxy-phenyl)-3,4-dihydro-1H-isoquinolin-2-yl]-ethyl}-diethyl-
 amine;
 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-
 imidazol-1-yl)-ethanone;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester;
- 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazol-1-yl)-2,2-dimethyl-propan-1-one;
- 1-(5-Bromo-2-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
- 10 1-(2-Methoxy-benzyl)-2-methyl-2,3-dihydro-1H-isoindole;
- 2-Methyl-1-naphthalen-1-ylmethyl-2,3-dihydro-1H-isoindole;
- 1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-2,2-dimethyl-propan-1-one;
- {2-[1-(5-Bromo-2-methoxy-benzyl)-1,3-dihydro-isoindol-2-yl]-ethyl}-diethyl-amine;
- 15 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid tert-butyl ester;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 20 1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-ethanone;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
- 25 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
- 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-N-(3-formylamino-propyl)-6-methyl-benzamide;
- 30 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-ethyl-4,5-dihydro-1H-imidazole;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-2,2-dimethyl-propan-1-one;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid isobutyl ester;
- 35 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isocyanomethyl-4,5-dihydro-1H-imidazole;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-methyl-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-ethyl-4,5-dihydro-1H-imidazole;
- 5 3-(5-Bromo-2-methoxy-benzyl)-2-methyl-2,3-dihydro-isoindol-1-one;
- 4-(2-Methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
- 4-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-propyl-4,5-dihydro-1H-imidazole;
- 10 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
- 5,5-Dimethyl-2-[2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
- 15 N-(5-Bromo-2-methoxy-benzyl)-N'-methyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-N,N,N'-trimethyl-benzamidine;
- 20 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
- 1-Benzyl-2-{2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;
- ((2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl)-pyrrolidin-1-yl-methylene)-methyl-amine;
- 25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isopropyl-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-(2,2,2-trifluoro-ethyl)-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-
- 30 pyrimidine, and pharmaceutically acceptable salts thereof.

Other compounds of the invention are shown in Table 4.

- In one further embodiment, the methods of the invention do not include methods wherein 2-[2-(2,5-dichlorothiophen-3-ylmethylsulfanyl)-phenyl]-1, 4, 5, 6-tetrahydropyrimidine (Compound A); 2[2-(2-chloro- 6-fluoro-benzylsulfanyl)-phenyl]-
- 35 1, 4, 5, 6-tetrahydropyrimidine (Compound B); 1-(6-bromo-2-chloro-quinolin-4-yl)-3-(2-diethylaminoethyl)-urea (Compound AN); 2-[2-(2,6-difluorobenzylsulfanyl)-phenyl]-1, 4, 5, 6-tetrahydropyrimidine (Compound AO); 1-(4-hydroxy-1, 3, 5-trimethyl-piperadin-4-yl)-ethanone (Compound AR); 4,6-dimethyl-2-piperazin-1-yl-pyrimidine

(Compound FP); 2-piperazin-1-yl-pyrimidine (Compound FR); 1-pyridin-2-yl-piperazine (Compound FS); 2-piperazin-1-yl-4-trifluoromethyl pyrimidine (Compound FT); 6-piperazin-1-yl-7-trifluoromethyl-thieno[3,2-b]pyridine-3-carboxylic acid methyl ester (Compound FU); 5-bromo-2-piperazin-1-yl-pyrimidine (Compound FV); 1-(3-trifluoromethyl-pyridin-2-yl)-piperazine (Compound FW); 1-(5-trifluoromethyl-pyridin-2-yl)-piperazine (Compound FX); piperazine (Compound KY); or (2-Hexyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester (Compound OQ) are used as MC4-R binding compounds. In another further embodiment, the compounds claimed as MC4-R binding compounds do not include those listed above.

10 In another embodiment, the methods of the invention do not include methods wherein 2-naphthalen-1-ylmethyl-4,5-dihydro-1H-imidazole (NAPHAZOLINE; Compound AS); 10-[2-(1-methyl-piperidin-2-yl)-ethyl]-2-methylsulfanyl-10H-phenothiazine (THORADIAZINE; THIODIAZINE; Compound AP); (2,6-dichloro-phenyl)-imidazolidin-2-ylidene-amine (CLONIDINE; Compound AY); or 2-benzyl-4,5-dihydro-1H-imidazole (TOLAZOLINE; Compound AZ) are used as MC4-R binding compounds. In another further embodiment, the invention pertains to compounds other than those listed above as MC4-R binding compounds.

In another further embodiment, the methods of the invention do not include 5-(4-chloro-phenyl)-2,5-dihydro-3H-imidazo[2,1-a]-isoindol-5-ol (MASPINDOL; Compound DT) as an MC4-R binding compound. In one embodiment, the compounds of the invention include MC4-R binding compounds other than MASPINDOL.

The term "alkyl" includes saturated aliphatic groups, including straight-chain alkyl groups (e.g., methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, etc.), branched-chain alkyl groups (isopropyl, tert-butyl, isobutyl, etc.), cycloalkyl (alicyclic) groups (cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl), alkyl substituted cycloalkyl groups, and cycloalkyl substituted alkyl groups. The term alkyl further includes alkyl groups, which can further include oxygen, nitrogen, sulfur or phosphorous atoms replacing one or more carbons of the hydrocarbon backbone. In an embodiment, a straight chain or branched chain alkyl has 10 or fewer carbon atoms in its backbone (e.g., C₁-C₁₀ for straight chain, C₃-C₁₀ for branched chain), and more preferably 6 or fewer. Likewise, preferred cycloalkyls have from 4-7 carbon atoms in their ring structure, and more preferably have 5 or 6 carbons in the ring structure.

Moreover, the term alkyl includes both "unsubstituted alkyls" and "substituted alkyls", the latter of which refers to alkyl moieties having substituents replacing a hydrogen on one or more carbons of the hydrocarbon backbone. Such substituents can include, for example, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl,

dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety. Cycloalkyls can be further substituted, e.g., with the substituents described above. An "alkylaryl" or an "aralkyl" moiety is an alkyl substituted with an aryl (e.g., phenylmethyl (benzyl)). The term "alkyl" also includes the side chains of natural and unnatural amino acids. Examples of halogenated alkyl groups include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, perfluoromethyl, perchloromethyl, perfluoroethyl, perchloroethyl, etc.

The term "aryl" includes groups, including 5- and 6-membered single-ring aromatic groups that may include from zero to four heteroatoms, for example, benzene, phenyl, pyrrole, furan, thiophene, thiazole, isothiazole, imidazole, imidazoline, triazole, tetrazole, pyrazole, oxazole, isooxazole, pyridine, pyrazine, pyridazine, and pyrimidine, and the like. Furthermore, the term "aryl" includes multicyclic aryl groups, e.g., tricyclic, bicyclic, e.g., naphthalene, benzoxazole, benzodioxazole, benzothiazole, benzoimidazole, benzothiophene, methylenedioxyphenyl, quinoline, isoquinoline, naphthridine, indole, benzofuran, purine, benzofuran, deazapurine, isoindole, indan or indolizine. Those aryl groups having heteroatoms in the ring structure may also be referred to as "aryl heterocycles", "heterocycles," "heteroaryls" or "heteroaromatics". The aromatic ring can be substituted at one or more ring positions with such substituents as described above, as for example, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy, carboxylate, alkylcarbonyl, alkylaminocarbonyl, aralkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety. Aryl groups can also be fused or bridged with alicyclic or heterocyclic rings which are not aromatic so as to form a polycycle (e.g., tetralin).

The term "alkenyl" includes unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but that contain at least one double bond.

For example, the term "alkenyl" includes straight-chain alkenyl groups (e.g., ethenyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, decenyl, etc.), branched-chain alkenyl groups, cycloalkenyl (alicyclic) groups (cyclopropenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl), alkyl or alkenyl substituted cycloalkenyl groups, and cycloalkyl or cycloalkenyl substituted alkenyl groups. The term alkenyl further includes alkenyl groups which include oxygen, nitrogen, sulfur or phosphorous atoms replacing one or more carbons of the hydrocarbon backbone. In certain embodiments, a straight chain or branched chain alkenyl group has 6 or fewer carbon atoms in its backbone (e.g., C₂-C₆ for straight chain, C₃-C₆ for branched chain). Likewise, cycloalkenyl groups may have from 3-8 carbon atoms in their ring structure, and more preferably have 5 or 6 carbons in the ring structure. The term C₂-C₆ includes alkenyl groups containing 2 to 6 carbon atoms.

Moreover, the term alkenyl includes both "unsubstituted alkenyls" and "substituted alkenyls", the latter of which refers to alkenyl moieties having substituents replacing a hydrogen on one or more carbons of the hydrocarbon backbone. Such substituents can include, for example, alkyl groups, alkynyl groups, halogens, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonate, phosphinate, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylaryl amino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

The term "alkynyl" includes unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but which contain at least one triple bond.

For example, the term "alkynyl" includes straight-chain alkynyl groups (e.g., ethynyl, propynyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, decynyl, etc.), branched-chain alkynyl groups, and cycloalkyl or cycloalkenyl substituted alkynyl groups. The term alkynyl further includes alkynyl groups which include oxygen, nitrogen, sulfur or phosphorous atoms replacing one or more carbons of the hydrocarbon backbone. In certain embodiments, a straight chain or branched chain alkynyl group has 6 or fewer carbon atoms in its backbone (e.g., C₂-C₆ for straight chain, C₃-C₆ for

branched chain). The term C₂-C₆ includes alkynyl groups containing 2 to 6 carbon atoms.

Moreover, the term alkynyl includes both "unsubstituted alkynyls" and "substituted alkynyls", the latter of which refers to alkynyl moieties having substituents replacing a hydrogen on one or more carbons of the hydrocarbon backbone. Such substituents can include, for example, alkyl groups, alkynyl groups, halogens, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonate, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

Unless the number of carbons is otherwise specified, "lower alkyl" as used herein means an alkyl group, as defined above, but having from one to five carbon atoms in its backbone structure. "Lower alkenyl" and "lower alkynyl" have chain lengths of, for example, 2-5 carbon atoms.

The term "acyl" includes compounds and moieties which contain the acyl radical (CH₃CO-) or a carbonyl group. The term "substituted acyl" includes acyl groups where one or more of the hydrogen atoms are replaced by for example, alkyl groups, alkynyl groups, halogens, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonate, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

The term "acylamino" includes moieties wherein an acyl moiety is bonded to an amino group. For example, the term includes alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido groups.

The term "aroyl" includes compounds and moieties with an aryl or heteroaromatic moiety bound to a carbonyl group. Examples of aroyl groups include phenylcarboxy, naphthyl carboxy, etc.

The terms "alkoxyalkyl", "alkylaminoalkyl" and "thioalkoxyalkyl" include alkyl groups, as described above, which further include oxygen, nitrogen or sulfur atoms replacing one or more carbons of the hydrocarbon backbone, e.g., oxygen, nitrogen or sulfur atoms.

5 The term "alkoxy" includes substituted and unsubstituted alkyl, alkenyl, and alkynyl groups covalently linked to an oxygen atom. Examples of alkoxy groups include methoxy, ethoxy, isopropoxy, propoxy, butoxy, and pentoxy groups and may include cyclic groups such as cyclopentoxy. Examples of substituted alkoxy groups include halogenated alkoxy groups. The alkoxy groups can be substituted with groups
10 such as alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxy, phosphate, phosphonate, phosphinate, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylarylamino),
15 acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonate, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moieties. Examples of halogen substituted alkoxy groups include, but are not limited to, fluoromethoxy, difluoromethoxy,
20 trifluoromethoxy, chloromethoxy, dichloromethoxy, trichloromethoxy, etc.

The term "amine" or "amino" includes compounds where a nitrogen atom is covalently bonded to at least one carbon or heteroatom such as alkyl aminos, alkenyl aminos, dialkyl aminos, aryl aminos, acyl aminos, etc. The term "alkyl amino" includes groups and compounds wherein the nitrogen is bound to at least one additional alkyl
25 group and is included in the term "amino." The term "dialkyl amino" includes groups wherein the nitrogen atom is bound to at least two additional alkyl groups and is included in the term "amino." The term "arylamino" and "diarylamino" include groups wherein the nitrogen is bound to at least one or two aryl groups, respectively, and are included in the term "amino." The term "alkylarylamino," "alkylaminoaryl" or
30 "arylaminoalkyl" refers to an amino group which is bound to at least one alkyl group and at least one aryl group. The term "alkaminoalkyl" refers to an alkyl, alkenyl, or alkynyl group bound to a nitrogen atom which is also bound to an alkyl group and is included in the term "amino."

The term "amide" or "aminocarboxy" includes compounds or moieties which
35 contain a nitrogen atom which is bound to the carbon of a carbonyl or a thiocarbonyl group. The term includes "alkaminocarboxy" groups which include alkyl, alkenyl, or alkynyl groups bound to an amino group bound to a carboxy group. It includes arylaminocarboxy groups which include aryl or heteroaryl moieties bound to an amino

group which is bound to the carbon of a carbonyl or thiocarbonyl group. The terms “alkylaminocarboxy,” “alkenylaminocarboxy,” “alkynylaminocarboxy,” and “arylaminocarboxy” include moieties wherein alkyl, alkenyl, alkynyl and aryl moieties, respectively, are bound to a nitrogen atom which is in turn bound to the carbon of a carbonyl group.

The term “carbonyl” or “carboxy” includes compounds and moieties which contain a carbon connected with a double bond to an oxygen atom, and tautomeric forms thereof. Examples of moieties which contain a carbonyl include aldehydes, ketones, carboxylic acids, amides, esters, anhydrides, etc. The term “carboxy moiety” or “carbonyl moiety” refers to groups such as “alkylcarbonyl” groups wherein an alkyl group is covalently bound to a carbonyl group, “alkenylcarbonyl” groups wherein an alkenyl group is covalently bound to a carbonyl group, “alkynylcarbonyl” groups wherein an alkynyl group is covalently bound to a carbonyl group, “arylcarbonyl” groups wherein an aryl group is covalently attached to the carbonyl group. Furthermore, the term also refers to groups wherein one or more heteroatoms are covalently bonded to the carbonyl moiety. For example, the term includes moieties such as, for example, aminocarbonyl moieties, (wherein a nitrogen atom is bound to the carbon of the carbonyl group, e.g., an amide), aminocarbonyloxy moieties, wherein an oxygen and a nitrogen atom are both bond to the carbon of the carbonyl group (e.g., also referred to as a “carbamate”). Furthermore, aminocarbonylamino groups (e.g., ureas) are also include as well as other combinations of carbonyl groups bound to heteroatoms (e.g., nitrogen, oxygen, sulfur, etc. as well as carbon atoms). Furthermore, the heteroatom can be further substituted with one or more alkyl, alkenyl, alkynyl, aryl, aralkyl, acyl, etc. moieties.

The term “thiocarbonyl” or “thiocarboxy” includes compounds and moieties which contain a carbon connected with a double bond to a sulfur atom. The term “thiocarbonyl moiety” includes moieties which are analogous to carbonyl moieties. For example, “thiocarbonyl” moieties include aminothiocabonyl, wherein an amino group is bound to the carbon atom of the thiocarbonyl group, furthermore other thiocarbonyl moieties include, oxythiocarbonyls (oxygen bound to the carbon atom), aminothiocabonylamino groups, etc.

The term “ether” includes compounds or moieties which contain an oxygen bonded to two different carbon atoms or heteroatoms. For example, the term includes “alkoxyalkyl” which refers to an alkyl, alkenyl, or alkynyl group covalently bonded to an oxygen atom which is covalently bonded to another alkyl group.

The term “ester” includes compounds and moieties which contain a carbon or a heteroatom bound to an oxygen atom which is bonded to the carbon of a carbonyl group. The term “ester” includes alkoxycarboxy groups such as methoxycarbonyl,

ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, pentoxycarbonyl, etc. The alkyl, alkenyl, or alkynyl groups are as defined above.

The term "thioether" includes compounds and moieties which contain a sulfur atom bonded to two different carbon or hetero atoms. Examples of thioethers include, but are not limited to alkthioalkyls, alkthioalkenyls, and alkthioalkynyls. The term "alkthioalkyls" include compounds with an alkyl, alkenyl, or alkynyl group bonded to a sulfur atom which is bonded to an alkyl group. Similarly, the term "alkthioalkenyls" and alkthioalkynyls" refer to compounds or moieties wherein an alkyl, alkenyl, or alkynyl group is bonded to a sulfur atom which is covalently bonded to an alkynyl group.

The term "thiol" includes groups with an -SH group. In certain embodiments, it may also include thioethers, thioalkyls, thioaryls, thiocarbonyls, as described above.

The term "hydroxy" or "hydroxyl" includes groups with an -OH or -O[•].

The term "halogen" includes fluorine, bromine, chlorine, iodine, etc. The term "perhalogenated" generally refers to a moiety wherein all hydrogens are replaced by halogen atoms.

The terms "polycyclyl" or "polycyclic radical" include moieties with two or more rings (e.g., cycloalkyls, cycloalkenyls, cycloalkynyls, aryls and/or heterocyclyls) in which two or more carbons are common to two adjoining rings, e.g., the rings are "fused rings". Rings that are joined through non-adjacent atoms are termed "bridged" rings. Each of the rings of the polycycle can be substituted with such substituents as described above, as for example, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, alkylaminoacarbonyl, aralkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, alkenylcarbonyl, aminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, cyano, amino (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylaryl amino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkyl, alkylaryl, or an aromatic or heteroaromatic moiety.

The term "heteroatom" includes atoms of any element other than carbon or hydrogen. Preferred heteroatoms are nitrogen, oxygen, sulfur and phosphorus.

The term "heterocycle" or "heterocyclic" includes saturated, unsaturated, aromatic ("heteroaryls" or "heteroaromatic") and polycyclic rings which contain one or more heteroatoms. Examples of heterocycles include, for example, benzodioxazole, benzofuran, benzoimidazole, benzothiazole, benzothiophene, benzoxazole, deazapurine, furan, indole, indolizine, imidazole, isooxazole, isoquinoline, isothiazole,

methylenedioxyphenyl, naphthridine, oxazole, purine, pyrazine, pyrazole, pyridazine, pyridine, pyrimidine, pyrrole, quinoline, tetrazole, thiazole, thiophene, and triazole. Other heterocycles include morpholine, piprazine, piperidine, thiomorpholine, and thioazolidine. The heterocycles may be substituted or unsubstituted. Examples of
5 substituents include, for example, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, carboxylate, alkylcarbonyl, alkoxycarbonyl, alkylaminoacarbonyl, aralkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, alkenylcarbonyl, aminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, cyano, amino
10 (including alkyl amino, dialkylamino, arylamino, diarylamino, and alkylaryl amino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkyl, alkylaryl, or an aromatic or heteroaromatic moiety.

15 It will be noted that the structure of some of the compounds of this invention includes asymmetric carbon atoms. It is to be understood accordingly that the isomers arising from such asymmetry (e.g., all enantiomers and diastereomers) are included within the scope of this invention, unless indicated otherwise. Such isomers can be obtained in substantially pure form by classical separation techniques and by
20 stereochemically controlled synthesis. Furthermore, the structures and other compounds and moieties discussed in this application also include all tautomers thereof.

In a further embodiment, the compound is an antagonist of the MC4-R. In another embodiment, the compound is an agonist of the MC4-R. Compounds which are agonists of MC4-R can be identified using the cAMP assay given in Example 5.

25 The term "administering" includes routes of administration which allow the MC4-R binding compound to perform its intended function, e.g. interacting with MC4-Rs and/or treating a MC4-R associated state. Examples of routes of administration which can be used include parental injection (e.g., subcutaneous, intravenous, and intramuscular), intraperitoneal injection, oral, inhalation, and transdermal. The injection
30 can be bolus injections or can be continuous infusion. Depending on the route of administration, the MC4-R binding compound can be coated with or disposed in a selected material to protect it from natural conditions which may detrimentally effect its ability to perform its intended function. The MC4-R binding compound can be administered alone or with a pharmaceutically acceptable carrier. Further, the MC4-R
35 binding compound can be administered as a mixture of MC4-R binding compounds, which also can be coadministered with a pharmaceutically acceptable carrier. The MC4-R binding compound can be administered prior to the onset of a MC4-R associated

state, or after the onset of a MC4-R associated state. The MC4-R binding compound also can be administered as a prodrug which is converted to another form *in vivo*.

In one embodiment of the invention, the invention includes methods of treating an MC4-R associated state by administering the MC4-R binding compound of the invention in combination with art recognized compounds, e.g., therapeutic agents. For example, a patient suffering from cachexia resulting from HIV, may be treated using both the MC4-R binding compounds of the invention in combination with art recognized compounds for treating the cachexia or HIV itself. The term "combination with" includes both simultaneous administration as well as administration of the MC4-R binding compound before the art recognized compound or after the compound. The period between administrations of the MC4-R binding compound and the other agent may be any length of time which allows the compositions to perform their intended function, e.g., the interval may be between few minutes, an hour, more than one hour, etc. In addition, the MC4-R binding compounds may also be administered in combination with other MC4-R binding compounds of the invention.

The invention also features a pharmaceutical composition for the treatment of a MC4-R associated state in a mammal. The pharmaceutical composition includes a pharmaceutically acceptable carrier and an effective amount of an MC4-R binding compound of the formula (I):

20

B-Z-E**(I)**

wherein B is an anchor moiety, Z is a central moiety, and E is a MC4-R interacting moiety. In other embodiments, the pharmaceutical compositions of the invention include MC4-R binding compounds of formulae II, III, IV, V, VI, VII, VIII, IX, X, and/or XI. Pharmaceutical compositions comprising pharmaceutically acceptable salts of at least one MC4-R binding compound are also included.

The language "effective amount" of the compound is that amount necessary or sufficient to treat or prevent a MC4-R associated state, e.g. prevent the various morphological and somatic symptoms of a MC4-R associated state. The effective amount can vary depending on such factors as the size and weight of the subject, the type of illness, or the particular MC4-R binding compound. For example, the choice of the MC4-R binding compound can affect what constitutes an "effective amount". One of ordinary skill in the art would be able to study the aforementioned factors and make the determination regarding the effective amount of the MC4-R binding compound without undue experimentation. An *in vivo* assay as described in Example 4 below or an assay similar thereto (e.g., differing in choice of cell line or type of illness) also can be used to determine an "effective amount" of a MC4-R binding compound. The ordinarily

35

skilled artisan would select an appropriate amount of a MC4-R binding compound for use in the aforementioned *in vivo* assay. Advantageously, the effective amount is effective to treat a disorder associated with pigmentation, bones (e.g., osteoporosis, osteogenesis imperfecta (brittle bone disease), hypophosphatasia, Paget's disease, fibrous dysplasia, osteopetrosis, myeloma bone disease, bone formation, bone remodeling, bone healing, or the depletion of calcium in bone, such as that which is related to primary hyperparathyroidism) or weight loss, e.g., weight loss is a result of anorexia nervosa, old age, cancer cachexia, or HIV cachexia.

The regimen of administration can affect what constitutes an effective amount. The MC4-R binding compound can be administered to the subject either prior to or after the onset of a MC4-R associated state. Further, several divided dosages, as well as staggered dosages, can be administered daily or sequentially, or the dose can be continuously infused, or can be a bolus injection. Further, the dosages of the MC4-R binding compound(s) can be proportionally increased or decreased as indicated by the exigencies of the therapeutic or prophylactic situation.

The term "treated," "treating" or "treatment" includes the diminishment or alleviation of at least one symptom associated or caused by the state, disorder or disease being treated. For example, treatment can be diminishment of one or several symptoms of a disorder or complete eradication of a disorder.

The language "pharmaceutical composition" includes preparations suitable for administration to mammals, e.g., humans. When the compounds of the present invention are administered as pharmaceuticals to mammals, e.g., humans, they can be given per se or as a pharmaceutical composition containing, for example, 0.1 to 99.5% (more preferably, 0.5 to 90%) of active ingredient in combination with a pharmaceutically acceptable carrier.

The phrase "pharmaceutically acceptable carrier" is art recognized and includes a pharmaceutically acceptable material, composition or vehicle, suitable for administering compounds of the present invention to mammals. The carriers include liquid or solid filler, diluent, excipient, solvent or encapsulating material, involved in carrying or transporting the subject agent from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene

glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; phosphate buffer solutions; and other non-toxic compatible
5 substances employed in pharmaceutical formulations.

Wetting agents, emulsifiers and lubricants, such as sodium lauryl sulfate and magnesium stearate, as well as coloring agents, release agents, coating agents, sweetening, flavoring and perfuming agents, preservatives and antioxidants can also be present in the compositions.

10 Examples of pharmaceutically acceptable antioxidants include: water soluble antioxidants, such as ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite and the like; oil-soluble antioxidants, such as ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, α -tocopherol, and the like; and metal chelating agents, such as citric acid,
15 ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, and the like.

Formulations of the present invention include those suitable for oral, nasal, topical, transdermal, buccal, sublingual, rectal, vaginal and/or parenteral administration. The formulations may conveniently be presented in unit dosage form and may be
20 prepared by any methods well known in the art of pharmacy. The amount of active ingredient which can be combined with a carrier material to produce a single dosage form will generally be that amount of the compound which produces a therapeutic effect. Generally, out of one hundred per cent, this amount will range from about 1 per cent to about ninety-nine percent of active ingredient, preferably from about 5 per cent
25 to about 70 per cent, most preferably from about 10 per cent to about 30 per cent.

Methods of preparing these formulations or compositions include the step of bringing into association a compound of the present invention with the carrier and, optionally, one or more accessory ingredients. In general, the formulations are prepared by uniformly and intimately bringing into association a compound of the present
30 invention with liquid carriers, or finely divided solid carriers, or both, and then, if necessary, shaping the product.

Formulations of the invention suitable for oral administration may be in the form of capsules, cachets, pills, tablets, lozenges (using a flavored basis, usually sucrose and acacia or tragacanth), powders, granules, or as a solution or a suspension in an aqueous
35 or non-aqueous liquid, or as an oil-in-water or water-in-oil liquid emulsion, or as an elixir or syrup, or as pastilles (using an inert base, such as gelatin and glycerin, or sucrose and acacia) and/or as mouth washes and the like, each containing a predetermined amount of a compound of the present invention as an active ingredient. A

compound of the present invention may also be administered as a bolus, electuary or paste.

In solid dosage forms of the invention for oral administration (capsules, tablets, pills, dragees, powders, granules and the like), the active ingredient is mixed with one or
5 more pharmaceutically acceptable carriers, such as sodium citrate or dicalcium phosphate, and/or any of the following: fillers or extenders, such as starches, lactose, sucrose, glucose, mannitol, and/or silicic acid; binders, such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinyl pyrrolidone, sucrose and/or acacia; humectants, such as glycerol; disintegrating agents, such as agar-agar, calcium
10 carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate; solution retarding agents, such as paraffin; absorption accelerators, such as quaternary ammonium compounds; wetting agents, such as, for example, cetyl alcohol and glycerol monostearate; absorbents, such as kaolin and bentonite clay; lubricants, such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof; and coloring agents. In the case of capsules, tablets and pills, the
15 pharmaceutical compositions may also comprise buffering agents. Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugars, as well as high molecular weight polyethylene glycols and the like.

20 A tablet may be made by compression or molding, optionally with one or more accessory ingredients. Compressed tablets may be prepared using binder (for example, gelatin or hydroxypropylmethyl cellulose), lubricant, inert diluent, preservative, disintegrant (for example, sodium starch glycolate or cross-linked sodium carboxymethyl cellulose), surface-active or dispersing agent. Molded tablets may be
25 made by molding in a suitable machine a mixture of the powdered compound moistened with an inert liquid diluent.

The tablets, and other solid dosage forms of the pharmaceutical compositions of the present invention, such as dragees, capsules, pills and granules, may optionally be scored or prepared with coatings and shells, such as enteric coatings and other coatings
30 well known in the pharmaceutical-formulating art. They may also be formulated so as to provide slow or controlled release of the active ingredient therein using, for example, hydroxypropylmethyl cellulose in varying proportions to provide the desired release profile, other polymer matrices, liposomes and/or microspheres. They may be sterilized by, for example, filtration through a bacteria-retaining filter, or by incorporating
35 sterilizing agents in the form of sterile solid compositions which can be dissolved in sterile water, or some other sterile injectable medium immediately before use. These compositions may also optionally contain opacifying agents and may be of a composition that they release the active ingredient(s) only, or preferentially, in a certain

portion of the gastrointestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes. The active ingredient can also be in micro-encapsulated form, if appropriate, with one or more of the above-described excipients.

5 Liquid dosage forms for oral administration of the compounds of the invention include pharmaceutically acceptable emulsions, microemulsions, solutions, suspensions, syrups and elixirs. In addition to the active ingredient, the liquid dosage forms may contain inert diluent commonly used in the art, such as, for example, water or other solvents, solubilizing agents and emulsifiers, such as ethyl alcohol, isopropyl alcohol,
10 ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan, and mixtures thereof.

 Besides inert dilutents, the oral compositions can also include adjuvants such as
15 wetting agents, emulsifying and suspending agents, sweetening, flavoring, coloring, perfuming and preservative agents.

 Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-
20 agar and tragacanth, and mixtures thereof.

 Formulations of the pharmaceutical compositions of the invention for rectal or vaginal administration may be presented as a suppository, which may be prepared by mixing one or more compounds of the invention with one or more suitable nonirritating excipients or carriers comprising, for example, cocoa butter, polyethylene glycol, a
25 suppository wax or a salicylate, and which is solid at room temperature, but liquid at body temperature and, therefore, will melt in the rectum or vaginal cavity and release the active compound.

 Formulations of the present invention which are suitable for vaginal administration also include pessaries, tampons, creams, gels, pastes, foams or spray
30 formulations containing such carriers as are known in the art to be appropriate.

 Dosage forms for the topical or transdermal administration of a compound of this invention include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically acceptable carrier, and with any preservatives, buffers, or propellants
35 which may be required.

The ointments, pastes, creams and gels may contain, in addition to an active compound of this invention, excipients, such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof.

5 Powders and sprays can contain, in addition to a compound of this invention, excipients such as lactose, talc, silicic acid, aluminum hydroxide, calcium silicates and polyamide powder, or mixtures of these substances. Sprays can additionally contain customary propellants, such as chlorofluorohydrocarbons and volatile unsubstituted hydrocarbons, such as butane and propane.

10 Transdermal patches have the added advantage of providing controlled delivery of a compound of the present invention to the body. Such dosage forms can be made by dissolving or dispersing the compound in the proper medium. Absorption enhancers can also be used to increase the flux of the compound across the skin. The rate of such flux can be controlled by either providing a rate controlling membrane or dispersing the
15 active compound in a polymer matrix or gel.

Ophthalmic formulations, eye ointments, powders, solutions and the like, are also contemplated as being within the scope of this invention.

Pharmaceutical compositions of this invention suitable for parenteral administration comprise one or more compounds of the invention in combination with
20 one or more pharmaceutically acceptable sterile isotonic aqueous or nonaqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions just prior to use, which may contain antioxidants, buffers, bacteriostats, solutes which render the formulation isotonic with the blood of the intended recipient or suspending or thickening agents.

25 Examples of suitable aqueous and nonaqueous carriers which may be employed in the pharmaceutical compositions of the invention include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol, and the like), and suitable mixtures thereof, vegetable oils, such as olive oil, and injectable organic esters, such as ethyl oleate. Proper fluidity can be maintained, for example, by the use of coating
30 materials, such as lecithin, by the maintenance of the required particle size in the case of dispersions, and by the use of surfactants.

These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms may be ensured by the inclusion of various antibacterial and antifungal
35 agents, for example, paraben, chlorobutanol, phenol sorbic acid, and the like. It may also be desirable to include isotonic agents, such as sugars, sodium chloride, and the like into the compositions. In addition, prolonged absorption of the injectable pharmaceutical

form may be brought about by the inclusion of agents which delay absorption such as aluminum monostearate and gelatin.

In some cases, in order to prolong the effect of a drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This may be accomplished by the use of a liquid suspension of crystalline or amorphous material having poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally-administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

Injectable depot forms are made by forming microencapsule matrices of the subject compounds in biodegradable polymers such as polylactide-polyglycolide. Depending on the ratio of drug to polymer, and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions which are compatible with body tissue.

The preparations of the present invention may be given orally, parenterally, topically, or rectally. They are of course given by forms suitable for each administration route. For example, they are administered in tablets or capsule form, by injection, inhalation, eye lotion, ointment, suppository, etc. administration by injection, infusion or inhalation; topical by lotion or ointment; and rectal by suppositories. Oral administration is preferred.

The phrases "parenteral administration" and "administered parenterally" as used herein means modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal and intrasternal injection and infusion.

The phrases "systemic administration," "administered systemically," "peripheral administration" and "administered peripherally" as used herein mean the administration of a compound, drug or other material other than directly into the central nervous system, such that it enters the patient's system and, thus, is subject to metabolism and other like processes, for example, subcutaneous administration.

These compounds may be administered to humans and other animals for therapy by any suitable route of administration, including orally, nasally, as by, for example, a spray, rectally, intravaginally, parenterally, intracisternally and topically, as by powders, ointments or drops, including buccally and sublingually.

Regardless of the route of administration selected, the compounds of the present invention, which may be used in a suitable hydrated form, and/or the pharmaceutical compositions of the present invention, are formulated into pharmaceutically acceptable dosage forms by conventional methods known to those of skill in the art.

5 Actual dosage levels of the active ingredients in the pharmaceutical compositions of this invention may be varied so as to obtain an amount of the active ingredient which is effective to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient.

10 The selected dosage level will depend upon a variety of factors including the activity of the particular compound of the present invention employed, or the ester, salt or amide thereof, the route of administration, the time of administration, the rate of excretion of the particular compound being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular compound employed, the age, sex, weight, condition, general health and prior medical
15 history of the patient being treated, and like factors well known in the medical arts.

 A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the compounds of the invention employed in the pharmaceutical composition at levels lower than that required
20 in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved.

 In general, a suitable daily dose of a compound of the invention will be that amount of the compound which is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above.
25 Generally, intravenous and subcutaneous doses of the compounds of this invention for a patient, when used for the indicated analgesic effects, will range from about 0.0001 to about 100 mg per kilogram of body weight per day, more preferably from about 0.01 to about 50 mg per kg per day, and still more preferably from about 1.0 to about 100 mg per kg per day. An effective amount is that amount treats an MC4-R associated state.

30 If desired, the effective daily dose of the active compound may be administered as two, three, four, five, six or more sub-doses administered separately at appropriate intervals throughout the day, optionally, in unit dosage forms.

 While it is possible for a compound of the present invention to be administered alone, it is preferable to administer the compound as a pharmaceutical composition.

35 As set out above, certain embodiments of the present compounds can contain a basic functional group, such as amino or alkylamino, and are, thus, capable of forming pharmaceutically acceptable salts with pharmaceutically acceptable acids. The term "pharmaceutically acceptable salts" is art recognized and includes relatively non-toxic,

inorganic and organic acid addition salts of compounds of the present invention. These salts can be prepared *in situ* during the final isolation and purification of the compounds of the invention, or by separately reacting a purified compound of the invention in its free base form with a suitable organic or inorganic acid, and isolating the salt thus

5 formed. Representative salts include the hydrobromide, hydrochloride, sulfate, bisulfate, phosphate, nitrate, acetate, valerate, oleate, palmitate, stearate, laurate, benzoate, lactate, phosphate, tosylate, citrate, maleate, fumarate, succinate, tartrate, naphthylate, mesylate, glucoheptonate, lactobionate, and laurylsulphonate salts and the like. (See, *e.g.*, Berge et al. (1977) "Pharmaceutical Salts", *J. Pharm. Sci.* 66:1-19).

10 In other cases, the compounds of the present invention may contain one or more acidic functional groups and, thus, are capable of forming pharmaceutically acceptable salts with pharmaceutically acceptable bases. The term "pharmaceutically acceptable salts" in these instances includes relatively non-toxic, inorganic and organic base addition salts of compounds of the present invention. These salts can likewise be

15 prepared *in situ* during the final isolation and purification of the compounds, or by separately reacting the purified compound in its free acid form with a suitable base, such as the hydroxide, carbonate or bicarbonate of a pharmaceutically acceptable metal cation, with ammonia, or with a pharmaceutically acceptable organic primary, secondary or tertiary amine. Representative alkali or alkaline earth salts include the lithium,

20 sodium, potassium, calcium, magnesium, and aluminum salts and the like. Representative organic amines useful for the formation of base addition salts include ethylamine, diethylamine, ethylenediamine, ethanolamine, diethanolamine, piperazine and the like.

The term "pharmaceutically acceptable esters" refers to the relatively non-toxic,

25 esterified products of the compounds of the present invention. These esters can be prepared *in situ* during the final isolation and purification of the compounds, or by separately reacting the purified compound in its free acid form or hydroxyl with a suitable esterifying agent. Carboxylic acids can be converted into esters *via* treatment with an alcohol in the presence of a catalyst. Hydroxyls can be converted into esters *via*

30 treatment with an esterifying agent such as alkanoyl halides. The term also includes lower hydrocarbon groups capable of being solvated under physiological conditions, *e.g.*, alkyl esters, methyl, ethyl and propyl esters. (See, for example, Berge et al., *supra*.) A preferred ester group is an acetomethoxy ester group. Preferably, the amount of the MC4-R binding compound is effective to treat a pigmentation or weight loss

35 disorder, *e.g.*, weight loss associated with anorexia nervosa, old age, cachexia, HIV or cancer.

The invention also pertains to packaged MC4-R binding compounds. The packaged MC4-R binding compounds include, an MC4-R binding compound (e.g., of formulae I, II, III, IV, V, VI, VII, VIII, IX, X, and/or XI), a container, and directions for using said MC4-R binding compound to treat an MC4-R associated state, e.g., weight
 5 loss, etc.

Examples of MC4-R binding compounds for inclusion in pharmaceutical compositions include, for example,

- 2-[2-(4-benzyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2,5-dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[2-(2-methoxy-5-nitro-benzyloxy)-phenyl]-1,4,5,6-tetrahydropyrimidine;
- 2-[2-(2-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
- 2-{2-[2-(2-methoxy-naphthalen-1-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
- 2-[2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
- 2-{2-[2-(2-methyl-naphthalen-1-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
- 25 2-{2-[2-(2,3-dihydro-benzo[1,4]dioxin-5-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
- 2-[2-(2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
- 2-(2-Benzylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 2-(2-Pentadecylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 30 2-(2-Cyclohexylmethylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-Nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3,5-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(4-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 35 2-[2-(2-Chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2,4-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(3,5-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-nitro-benzylloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-(2-Benzylsulfanyl-phenyl)-4,5-dihydro-1H-imidazole;
- 5 2-[2-(2,6-Difluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(Naphthalen-1-ylmethoxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-{2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-
 ethanone;
- 10 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-
 benzoimidazole;
 2-[2-(2-Iodo-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
 2-[2-(2,5-Dimethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 4-[2-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-quinoline;
- 15 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-pyridin-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Cyclopentylloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 pyrimidine;
- 20 2-[2-(6-Methoxy-2,3-dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-
 tetrahydro-pyrimidine;
 2-[2-(5-fluoro-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 1-Methyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 25 2-[2-(5-Bromo-2-methoxy-benzylloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(Naphthalen-1-ylloxymethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-
 pyrimidine;
- 30 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-
 imidazole;
 2-[2-(2,6-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Bromo-6-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 35 pyrimidine;
 2-[4-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 pyrimidine;
 2-[2-(2-Bromo-5-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(Biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Chloro-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(2-Methoxy-5-thiophen-3-yl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(Biphenyl-2-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Iodo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-1,4,5,6-tetrahydro-
- 10 pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(4,4'-Dimethoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(9H-Fluoren-9-ylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(3'-Chloro-4'-fluoro-4-methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(1-Naphthalen-1-yl-ethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-4,5-dihydro-1H-imidazole;
- 20 2-(2-Benzhydrylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2'-Fluoro-4"-methoxy-[1,1';4',1"]terphenyl-3"-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzamidine;
- 2-[4-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 25 2-[2-(5-Ethynyl-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-cyclopentyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-ethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 30 2-[2-(5-Bromo-2-propoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperazine;
- C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-morpholin-2-yl}-methylamine;
- 35 2-[2-(2-Methoxy-5-methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylloxymethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-dimethyl-amine;
- 2-[2-(5-Bromo-2-isopropoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(2-Ethoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Propoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-benzonitrile;
- 5 1-{4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-phenyl}-ethanone;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;
 C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-
- 10 methylamine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,5,6,7,8,8a-hexahydroimidazo[1,5-a]pyridine;
- 15 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole;
 2-[2-(Benzo[b]thiophen-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Fluoro-2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-(Naphthalen-1-ylmethylsulfanyl)-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
- 20 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-3-methyl-butan-1-one;
- 25 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-2-phenyl-ethanone;
 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyridin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 N-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-guanidine;
 2-[2-(2-Isopropoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
- 30 pyrimidine;
 2-[2-(2-Cyclopentyloxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 (5-Bromo-2-methoxy-benzyl)-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-
- 35 pyrimidine;
 2-[2-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(6-Bromo-2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Chloro-2-(2-methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-
 5 pyrimidine;
 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 10 2-[1-(2-Naphthalen-1-yl-ethyl)-1H-pyrrol-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 (5-Bromo-2-methoxy-benzyl)-methyl-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine;
 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamine;
 2-[2-(2-Chloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 15 2-[2-(2-Bromo-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-(2-o-Tolylsulfanylmethyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,5-Dichloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-(3-Amino-propylamino)-6-(5-bromo-2-methoxy-benzylsulfanyl)-benzonitrile;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;
 20 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-morpholine;
 3'-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl;
 2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-piperazin-1-yl-6,7-dihydro-quinoline;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;
 25 C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-methylamine;
 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-pyrrolidin-3-ylamine;
 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-pyrrolidin-3-ylamine;
 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
 30 C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-morpholin-3-yl}-methylamine;
 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-azetidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ol;
 35 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester;
 [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester;

- [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-2-yl}-methanol;
- 5 4-tert-Butyl-N-naphthalen-1-ylmethyl-N-(2-piperidin-1-yl-ethyl)-benzamide;
 N,N-Dimethyl-N'-naphthalen-2-ylmethyl-N'-naphthalen-1-ylmethyl-propane-1,3-diamine;
 N-(5-Bromo-2-methoxy-benzyl)-N',N'-dimethyl-N-naphthalen-1-ylmethyl-propane-1,3-diamine;
- 10 1-Naphthalen-1-ylmethyl-3-phenethyl-1-(2-piperidin-1-yl-ethyl)-thiourea;
 3-(4-Dimethylamino-phenyl)-1-(3-dimethylamino-propyl)-1-naphthalen-1-ylmethyl-thiourea;
 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzylamino]-piperidine-1-carboxylic acid ethyl ester;
- 15 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethylamine;
 Naphthalene-2-sulfonic acid (2-dimethylamino-ethyl)-naphthalen-1-ylmethyl-amide;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-2-methoxymethyl-pyrrolidine;
 (2-Hexyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester;
- 20 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-pyrrolidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-piperidine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-propan-1-ol;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-3-methyl-butan-1-ol;
- 25 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ol;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-2-yl}-methanol;
 {1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-ethyl-N-pyrrolidine;
 N-pyrrolyl-[1-(2-naphthalen-1-yl-ethyl)-pyrrolidin-2-ylmethyl]-amine;
- 30 1-(2-Naphthalen-1-yl-ethyl)-piperidine-2-carboxylic acid methyl ester;
 (3-Bromo-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-amine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-piperidine;
 (5-Bromo-2-methoxy-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-amine;
- 35 (1-Ethyl-pyrrolidin-2-ylmethyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
 (3-Bromo-benzyl)-(3-imidazol-1-yl-propyl)-naphthalen-1-ylmethyl-amine;
 (3-Imidazol-1-yl-propyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;

- [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester;
 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-dimethylamino-ethyl ester;
 1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 5 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-amine;
 1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 N,N-Dimethyl-N'-(2-naphthalen-1-yl-ethyl)-N'-naphthalen-1-ylmethyl-ethane-1,2-diamine;
 10 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 {1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 15 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 {1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperidin-2-yl}-methanol;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-pyrrolidin-3-ylamine;
 1-Phenyl-3-piperazin-1-yl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile;
 20 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(4-Methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-phenylethynyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 25 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,5-Dimethoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(4-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 30 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-(Naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 35 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-phenyl}-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[3-Bromo-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Methoxy-5-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[4-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Naphthalen-1-yl-ethyl)-3-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(6-Fluoro-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidin-2-yl}-methanol;
- 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-[3-(2-methyl-piperidin-1-yl)-propyl]-amine;
- 20 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ylamine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperazine;
- 5,5-Dimethyl-2-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 3-(2-Naphthalen-1-yl-ethyl)-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
- 30 Amino-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-acetonitrile;
- 1-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethane-1,2-diamine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 35 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-1-methyl-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-5,5-
- 10 dimethyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Methoxy-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-
- 15 pyrimidine;
- 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-chloro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
- 2-[2-(1-Methyl-2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 3-(5-Bromo-2-methoxy-benzylsulfanyl)-2-fluoro-4-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-
- 20 phenylamine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 25 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-fluoro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
- 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-
- 30 pyrimidin-5-ol;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-Chloro-6-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-ethyl}-phenol;
- 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidin-
- 35 5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-5-methyl-4,5-dihydro-1H-imidazole;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,4-dimethyl-4,5-dihydro-1H-imidazole;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-4-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
4,4-Dimethyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-4,5-dihydro-oxazole;
10 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-4-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[5-(5-Bromo-2-methoxy-benzyl)-2-methyl-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1,4,5,6-tetrahydro-pyrimidine;
15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
20 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
30 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-benzonitrile;
2-{3-Benzyloxy-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-butyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
35 2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;

- 2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-8-chloro-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isobutoxy-phenyl}-1,4,5,6-tetrahydro-
- 10 pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5-methoxy-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-
- 20 imidazole;
- 2-{2-[3-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-biphenyl-2-yl]-ethyl}-phenol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-4,5-dihydro-1H-imidazole;
- N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methoxy-benzamide;
- 25 N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzamide;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-2-methyl-propyl ester;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 30 3-(5-Bromo-2-methoxy-phenyl)-5-chloro-3,4-dihydro-isoquinolin-1-ylamine;
- 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(4-methoxy-benzyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5-methyl-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 35 2-[(5-Bromo-2-methoxy-phenyl)-(3-piperidin-1-yl-propylamino)-methyl]-3-chloro-6-methyl-phenol;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-4-methyl-piperazine;

- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-diethyl-amine;
 3-(5-Bromo-2-methoxy-phenyl)-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 5 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;
 10 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-methanol;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
 15 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
 20 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
 25 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidin-2-yl)-methanol;
 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-benzamide;
 30 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
 35 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;

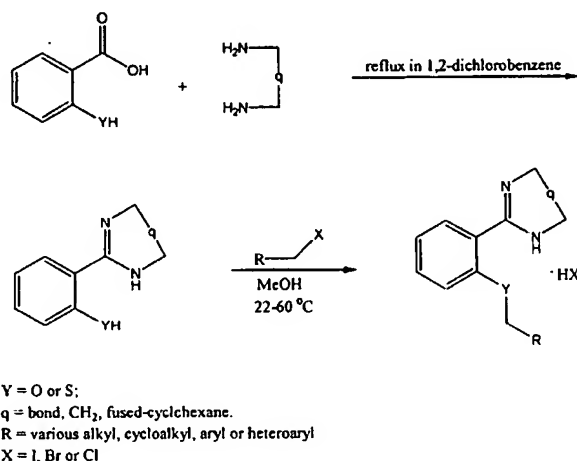
- (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-methanol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 5 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
- {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
- 10 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone;
- 15 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
- {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
- 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-benzamide;
- 20 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-4,5-dihydro-1H-imidazole;
- {2-[3-(5-Bromo-2-methoxy-phenyl)-3,4-dihydro-1H-isoquinolin-2-yl]-ethyl}-diethyl-amine;
- 25 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazol-1-yl)-ethanone;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-
- 30 1-carboxylic acid isobutyl ester;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazol-1-yl)-2,2-dimethyl-propan-1-one;
- 35 1-(5-Bromo-2-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
- 1-(2-Methoxy-benzyl)-2-methyl-2,3-dihydro-1H-isoindole;
- 2-Methyl-1-naphthalen-1-ylmethyl-2,3-dihydro-1H-isoindole;

- 1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-2,2-dimethyl-propan-1-one;
{2-[1-(5-Bromo-2-methoxy-benzyl)-1,3-dihydro-isoindol-2-yl]-ethyl}-diethyl-amine;
2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-1,4,5,6-tetrahydro-
5 pyrimidine;
2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid tert-butyl ester;
2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-
10 ethanone;
2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester;
2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
15 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-N-(3-formylamino-propyl)-6-methyl-benzamide;
2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-ethyl-4,5-dihydro-1H-imidazole;
20 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-2,2-dimethyl-propan-1-one;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-4,5-dihydro-1H-imidazole;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid isobutyl ester;
25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isocyanomethyl-4,5-dihydro-1H-imidazole;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-methyl-4,5-dihydro-1H-imidazole;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-ethyl-4,5-dihydro-1H-imidazole;
30 imidazole;
3-(5-Bromo-2-methoxy-benzyl)-2-methyl-2,3-dihydro-isoindol-1-one;
4-(2-Methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
4-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-propyl-4,5-dihydro-
35 1H-imidazole;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
5,5-Dimethyl-2-[2-(naphthalen-1-yl)sulfanylmethyl]-phenyl]-4,5-dihydro-1H-imidazole;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
 N-(5-Bromo-2-methoxy-benzyl)-N'-methyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine;
- 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-N,N,N'-trimethyl-benzamidine;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
 1-Benzyl-2-{2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;
- 10 ({2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-pyrrolidin-1-yl-methylene)-methyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isopropyl-4,5-dihydro-1H-imidazole;
- 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-(2,2,2-trifluoro-ethyl)-4,5-dihydro-1H-imidazole;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-pyrimidine, and pharmaceutically acceptable salts thereof. Also included are compositions containing the compounds listed in Table 4.
- 20 In a further embodiment, the pharmaceutical compositions of the invention include compositions wherein the MC4-R binding compound is not 5-(4-chloro-phenyl)-2,5-dihydro-3H-imidazo[2,1-a]-isoindol-5-ol (MASPINDOL; Compound DT).
- In another embodiment, the pharmaceutical compositions of the invention include compositions wherein the MC4-R binding compound is not 2-naphthalen-1-ylmethyl-4,5-dihydro-1H-imidazole (NAPHAZOLINE; Compound AS);
- 25 10-[2-(1-methyl-piperadin-2-yl)-ethyl]-2-methylsulfanyl-10H-phenothiazine (THORADIAZINE; THIODIAZINE; Compound AP); (2,6-dichloro-phenyl)-imidazolidin-2-ylidene-amine (CLONIDINE; Compound AY); or 2-benzyl-4,5-dihydro-1H-imidazole (TOLAZOLINE; Compound AZ).
- 30 In another further embodiment, the pharmaceutical compositions of the invention includes compositions wherein the MC4-R binding compound is not 2-[2-(2,5-dichlorothiophen-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine (Compound A); 2[2-(2-chloro-6-fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine (Compound B); 1-(6-bromo-2-chloro-quinolin-4-yl)-3-(2-diethylaminoethyl)-urea (Compound AN);
- 35 2-[2-(2,6-difluorobenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine (Compound AO); 1-(4-hydroxy-1,3,5-trimethyl-piperadin-4-yl)-ethanone (Compound AR); 4,6-dimethyl-2-piperazin-1-yl-pyrimidine (Compound FP); 2-piperazin-1-yl-pyrimidine (Compound FR); 1-pyridin-2-yl-piperazine

- (Compound FS); 2-piperazin-1-yl-4-trifluoromethyl pyrimidine (Compound FT); 6-piperazin-1-yl-7-trifluoromethyl-thieno[3,2-b]pyridine-3-carboxylic acid methyl ester (Compound FU); 5-bromo-2-piperazin-1-yl-pyrimidine (Compound FV); 1-(3-trifluoromethyl-pyridin-2-yl)-piperazine (Compound FW); 1-(5-trifluoromethyl-pyridin-2-yl)-piperazine (Compound FX); piperazine (Compound KY); or (2-Hexyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester (Compound OQ).

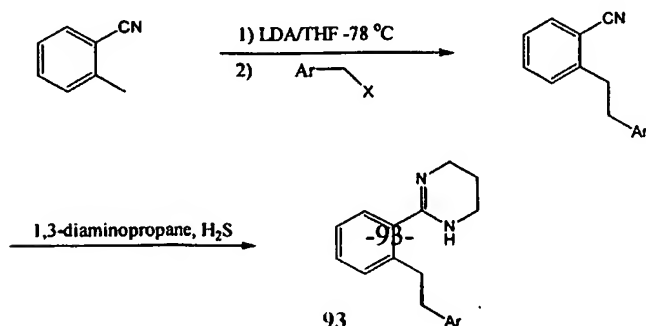
The compounds of the present invention can be synthesized using standard methods of chemical synthesis and/or can be synthesized using schemes described herein. Synthesis of specific compounds is discussed in detail in the Example sections below. Examples of syntheses of several classes of compounds of the invention are outlined in the schemes below. Scheme 1 depicts a method of synthesizing thiomethylene compound of the invention.



Scheme 1

- 2-hydroxy or 2-mercapto benzoic acid is heated with the diamine in refluxing 1,2-dichlorobenzene to form the corresponding heterocyclic compound. The desired thioether or ether is formed by treating the thiol or alcohol with a corresponding halogenated compound.

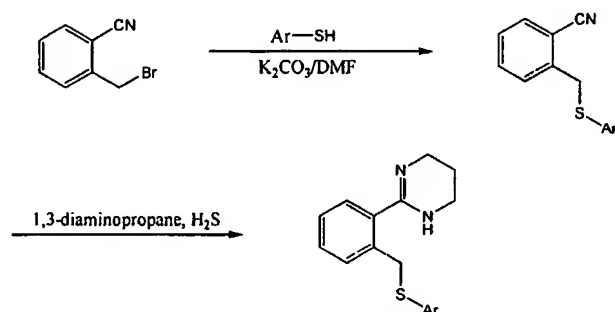
Scheme 2 depicts a general preparation of ethanyl-linked compounds of the invention.



Scheme 2

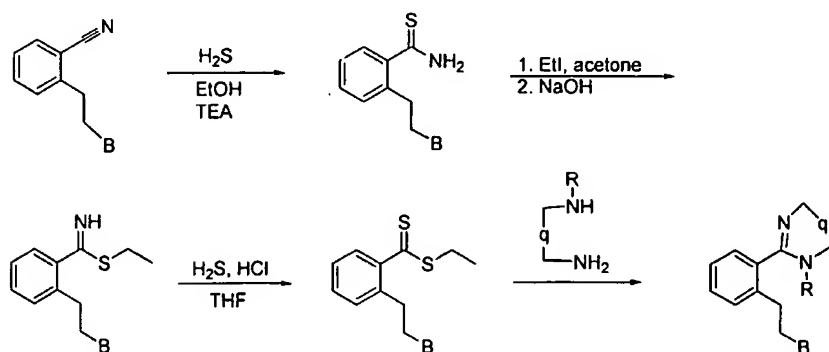
Scheme 2 shows a method of synthesizing ethanyl linked compounds by treating α -tolunitrile with a lithium base in THF at -78°C . A halogenated alkylaryl compound is then added to form the ethanyl linkage. To form the heterocycle, hydrogen sulfide gas is bubbled through a solution of the nitrile and 1,3 diaminopropane. After formation, the product can then be obtained and purified using standard techniques.

Scheme 3 depicts a method of preparing methylenethio linked compounds of the invention.



Scheme 3

As depicted in Scheme 3, the methylenethio compounds of the invention can be prepared by adding anhydrous K_2CO_3 to a thiophenol compound (Ar-SH) in DMF. The solution is then stirred and bromomethyl-benzonitrile is subsequently added. The thioether is then converted to the heterocyclic compound by bubbling hydrogen sulfide through a solution of the thioether and 1,3 diaminopropane. After formation, the product can then be obtained and purified using standard techniques.



Scheme 4

As depicted in Scheme 4, cyclic amidines of the invention can be prepared by reacting 2-substituted benzonitrile with hydrogen sulfide to form a thiobenzamide. The resulting thiobenzamide is then treated with iodoethane to give a

thiobenzimidic acid ethyl ester. In the presence of hydrochloric acid, the thiobenzimidic acid ethyl ester is suspended in tetrahydrofuran and treated with hydrogen sulfide. The resulting dithiobenzoic acid ethyl ester is then heated with various diamines, in the presence or absence of an added catalyst such as silver trifluoroacetate, to give cyclic
5 amidines.

The invention is further illustrated by the following examples which in no way should be construed as being further limiting. The contents of all references, pending patent applications and published patent applications, cited throughout this application are hereby incorporated by reference. It should be understood that the animal models
10 used throughout the examples are accepted animal models and that the demonstration of efficacy in these animal models is predictive of efficacy in humans.

EXEMPLIFICATION OF THE INVENTION:

15 EXAMPLE 1: Synthesis of Compounds B, HO, and IZ

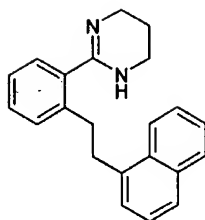
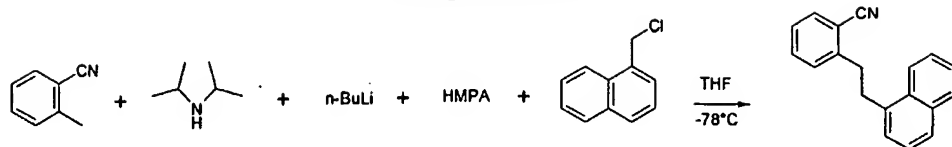
Synthesis of Compound B

2-(4,5-Dihydro-1H-imidazol-2-yl)-benzenethiol. To a suspension of 20.0 g (0.112 mol) of thiosalicylic acid in 200 mL of 1,2-dichlorobenzene was added 21.6 mL (0.323 mol)
20 of ethylenediamine. The mixture was refluxed under nitrogen for 4 h then cooled to ca. 60 °C and 50 mL of methanol was added. The solution was allowed to stand at 22 °C over night and the resulting yellow crystalline solid collected and washed with ether to give 10.6 g of pure product.

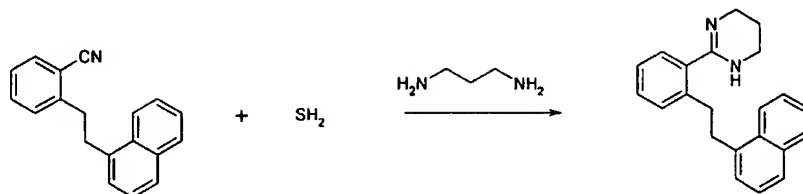
25 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrochloride (Compound B). To a solution of 750 mg (3.90 mmol) of 2-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-benzenethiol was added 1.04 g (5.81 mmol) of 1-Chloro-2-chloromethyl-3-fluoro-benzene. The solution was stirred overnight at 22 °C and 2-3 mL
30 of ether was added to induce crystallization. The crystals were collected and washed with ether to give 1.34 g of product.

NMR Data for Compound B

¹H NMR (300 MHz, CD₃OD) δ 2.01-2.09 (2H, m), 3.49 (4H, br t, J = 5.8 Hz), 4.28 (2H, s), 7.01-7.07 (1H, m), 7.22-7.33 (2H, m), 7.48 (2H, m), 7.56-7.64 (1H, m), 7.75 (1H, d, J
35 = 7.8 Hz)

Synthesis of Compound HO:**Compound HO****Scheme 5**

5 2-[(2-(2-Naphthalen-1-yl-ethyl)-phenyl)-1,4,5,6-tetrahydro-pyrimidin-2-yl]-1,4,5,6-tetrahydro-pyrimidine. A solution of 1.26 mL (911 mg, 9.00 mmol) of diisopropylamine in 50 mL of THF (tetrahydrofuran) was cooled to -78 °C under nitrogen and 5.6 mL (9.0 mmol) of *n*-butyllithium, 1.6 M in hexanes, was added via syringe. The mixture was stirred at -78 °C for 1 hour and a solution of 353 mg (3.00 mmol) of α -tolunitrile in 10 mL of THF was added. The solution was stirred at -78 °C for one additional hour and a solution of 1.57 mL (9.00 mmol) of HMPA and 583 mg (3.30 mmol) of 1-chloromethylnaphthalene in 10 mL of THF was added dropwise. After stirring for one additional hour at -78°C, the reaction was quenched with water and extracted with Et₂O (diethyl ether) (2x30 mL). The organic layer was washed with aqueous 1 N HCl (30mL), water (3x30mL), brine (30mL) and dried (Na₂SO₄). The solvent was evaporated to give 735 mg of crude product which was used directly in the next step.

**Scheme 6**

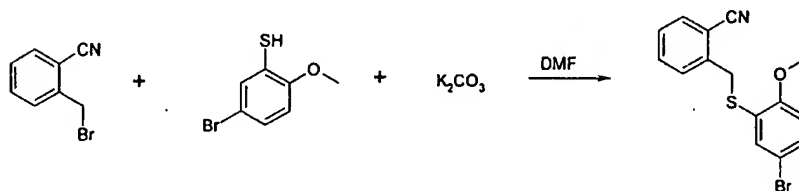
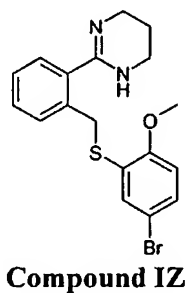
20 2-[(2-(2-Naphthalen-1-yl-ethyl)-phenyl)-1,4,5,6-tetrahydro-pyrimidin-2-yl]-1,4,5,6-tetrahydro-pyrimidine. Hydrogen sulfide gas was bubbled through a solution of 735 mg of crude 2-(2-Naphthalen-1-yl-ethyl)-benzonitrile in 5 mL of 1,3-diaminopropane for 5 minutes, as depicted in Scheme 6. The reaction was capped and heated to 80 °C for 72 hours. The reaction mixture was then diluted with 5 mL of water and extracted with ethyl acetate (2x10mL). The organic extracts were washed with water (3x10mL), brine (2x10mL), dried (Na₂SO₄) and the solvent was evaporated. The residue was purified on silica gel

(eluting with 90:10:1:1 of dichloromethane/methanol/water/formic acid) to afford 310 mg of the formate salt of the product as a colorless oil.

NMR Data for Compound HO:

- 5 ¹H NMR (300 MHz, CDCl₃) δ 1.35-1.50 (2H, m), 2.80-2.95 (4H, m), 3.03 (2H, t, J = 6.8), 3.30 (2H, t, J = 6.8), 6.77 (1H, d, J = 6.9), 7.03-7.30 (3H, m), 7.30-7.57 (4H, m), 7.67 (1H, d, J = 8.1), 7.80-7.90 (1H, m), 7.94-8.03 (1H, m), 8.06 (2H, brs, formate salt).

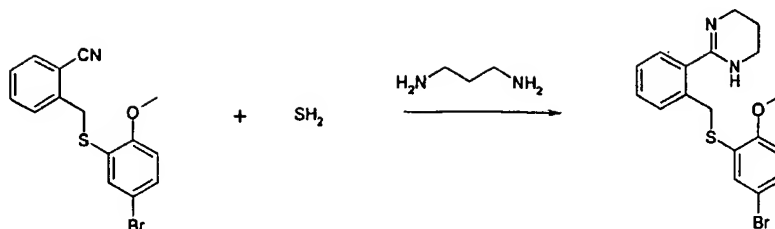
10 Synthesis of Compound IZ:



15

Scheme 7

- 2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-benzonitrile. As depicted in Scheme 7 above, to a solution of 104 mg (0.470 mmol) of 2-methoxy-5-bromo-thiophenol in 5 mL of DMF was added 162 mg (1.18 mmol) of anhydrous to a solution of 104 mg (0.470 mmol) of 2-methoxy-5-bromo-thiophenol in 5 mL of DMF was added 162 mg (1.18 mmol) of anhydrous K₂CO₃. The solution was stirred for 15 minutes at 22 °C and 103 mg (0.520 mmol) of 2-bromomethyl-benzonitrile was added. The reaction was capped and heated to 40 °C for 12 hours. The mixture was subsequently diluted with 5 mL of water and extracted with ethyl acetate (2x10mL). The organic extracts were washed with water (3x10mL), brine (2x10mL), and dried (Na₂SO₄). The solvent was evaporated and the product was purified on silica gel (eluting with 9:1 of hexane/ethyl acetate) to afford 102 mg of the product as a colorless oil.



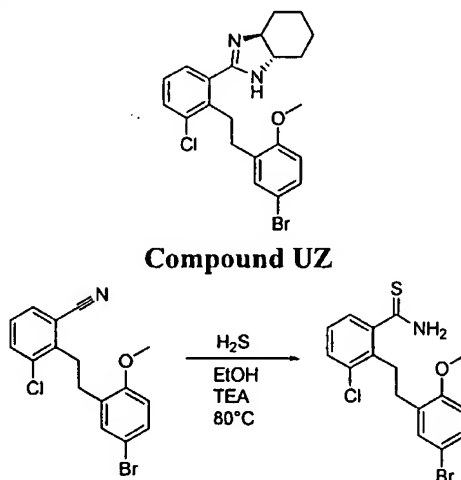
Scheme 8

2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine. (Compound DV) Compound DV was obtained from 2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-benzonitrile, 1,3-propanediamine and hydrogen sulfide in 73% yield by a procedure analogous to that used for the preparation of 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine described above. Following chromatography, the material was converted to the hydrochloride salt and recrystallized from methanol/ether.

10

NMR Data for Compound IZ

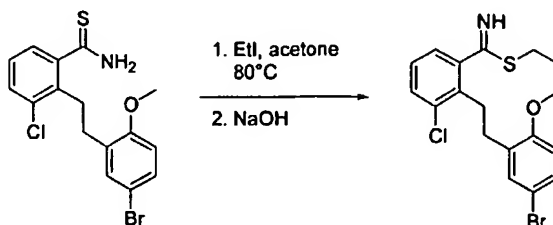
¹H NMR (300 MHz, DMSO-d₆) δ 1.95-2.10 (2H, m), 3.45-3.55 (4H, m), 3.86 (3H, s), 4.40 (2H, s), 6.97-7.04 (1H, m), 7.36-7.65 (6H, m), 10.03 (2H, s, hydrochloride salt).

15 **Synthesis of Compound UZ:**

Scheme 9

20 9, 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-thiobenzamide. As shown in Scheme 9, hydrogen sulfide gas was bubbled into a solution of 2.75 g (7.8 mmol) of 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzonitrile in 20 mL of ethanol and triethylamine (5:4 v/v) for 10 minutes. The solution was then heated to 80 °C in a sealed pressure tube for 5 hours. The reaction mixture was diluted with water and
25 extracted with ethyl acetate twice. The organic extracts were washed with brine, dried

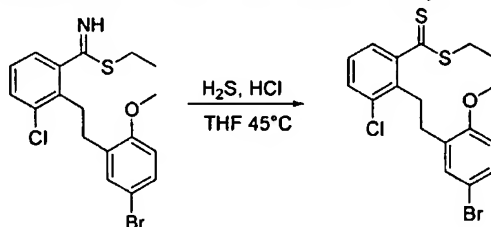
(MgSO₄), filtered and evaporated to give 3.0 g of crude product which was used directly in the next step.



Scheme 10

5 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-thiobenzimidic acid ethyl ester.

To a solution of 3.0 g (7.8 mmol) of 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-thiobenzamide in 50 mL of acetone was added 6 mL (75 mmol) of iodoethane (Scheme 10). The reaction was heated to 80 °C for 2 hours and then stirred at room temperature overnight. A white solid precipitated out of the solution and was filtered to give 3.23 g of the iodide salt. The salt was neutralized by partitioning between CH₂Cl₂ and 1 N aqueous sodium hydroxide. After drying (MgSO₄) and evaporation of the organic layer, 2.8 g of crude powder was obtained which was used directly in the next step.

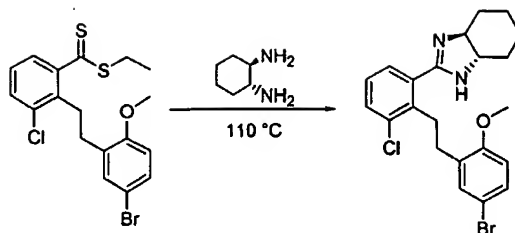


Scheme 11

15

2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-dithiobenzoic acid ethyl ester.

As shown in Scheme 11, hydrogen sulfide gas (~2 mL) was condensed into a cooled (-78 °C) solution of 2.8 grams (6.8 mmol) of 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-thiobenzimidic acid ethyl ester and 13.6 mL (13.6 mmol) of 1.0 M HCl/ether in 100 mL of tetrahydrofuran. The reaction was heated to 45 °C and stirred overnight in a sealed tube. The reaction mixture was diluted with water and extracted with methylene chloride once. The organic layer was washed with brine, dried (MgSO₄), filtered and evaporated to give a crude orange oil. The oil was partially purified by chromatography through a short column of silica gel (eluting with 5:95 ethyl acetate/hexanes) which resulted in 1.8 g of an orange powder which was used directly in the next step.



Scheme 12

2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole (Compound UZ). As shown in Scheme 12, a solution of 187 mg (0.43 mmol) of 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-dithiobenzoic acid ethyl ester in 2.5 mL of *trans*-1,2 diaminocyclohexane was heated to 110 °C in a sealed pressure tube for 12 hours. The reaction mixture was diluted with water and extracted with methylene chloride twice. The organic extracts were washed with brine, dried (MgSO₄) and evaporated. The residue was chromatographed on silica gel (eluting with 95:5 CH₂Cl₂/methanol) to give a yellow oil. The oil was treated with methanolic HCl and evaporated to yield 34 mg of product as a pure hydrochloride salt.

NMR Data for Compound UZ

¹H NMR (300 MHz, CD₃OD) δ 1.41-1.58 (2 H, br m), 1.64-1.80 (2 H, br m), 1.98 (2 H, br m), 2.30 (2 H, br m), 2.78-2.97 (2 H, m), 3.08 (1 H, m), 3.22-3.36 (1 H, m), 3.61 (2 H, m), 3.59 (3 H, s), 6.81 (1 H, d, *J* = 8.7 Hz), 7.21 (1 H, m), 7.34 (1 H, dd, *J* = 2.5, 8.6 Hz), 7.42 (2 H, m), 7.75 (1 H, dd, *J* = 2.3, 7.0 Hz).

The compounds given in Table 1, were made using procedures similar to that used for Compound B. The ES-LRMS values each had a relative intensity of 100.

Table 1: Physical Data of Selected MC4-R Binding Compounds

| ID | Name | Molecular Formula | Exact Mass (free Base) | ES-LRMS found (M+H) | Melt Point (°C) |
|----|---|---|------------------------|-----------------------|-----------------|
| I | 2-[2-(4-Benzyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrochloride | C ₂₄ H ₂₄ N ₂ OS HCl | 388.16 | 389.6 | 178-179 |
| M | 2-[2-(2-Iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrochloride | C ₁₇ H ₁₇ IN ₂ S HCl | 408.02 | 409 | 207-209 |
| N | 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrobromide | C ₁₈ H ₁₉ N ₃ O ₃ S HBr | 357.11 | 358.1 | 239-241 |
| O | 2-[2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrochloride | C ₂₁ H ₂₀ N ₂ S HCl | 332.13 | 333.1 | 207-208 |
| Q | 2-[2-(3-Chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrobromide | C ₁₇ H ₁₇ ClN ₂ S HBr | 316.08 | 317 | 224-225.5 |
| AI | 2-[2-(2,5-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrochloride | C ₁₉ H ₂₂ N ₂ O ₂ S HCl | 342.14 | 343.2 | 201-202 |
| Z | 2-[2-(3-Bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrobromide | C ₁₇ H ₁₇ BrN ₂ S HBr | 360.03 | 361 | 210-211 |
| B | 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrochloride | C ₁₇ H ₁₆ ClFN ₂ S HCl | 334.07 | 335 | 232-233 |
| AE | 2-[2-(2-Iodo-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole; hydrochloride | C ₁₆ H ₁₅ IN ₂ S HCl | 394 | 394.9 | 184-185 |
| AF | 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole; hydrobromide | C ₁₇ H ₁₇ N ₃ O ₃ HBr | 343.1 | 344.1 | 253-254 |
| Y | 2-[2-(2-Methoxy-5-nitro-benzyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrochloride | C ₁₈ H ₁₉ N ₃ O ₄ HCl | 341.14 | 342.1 | 220-221 |
| AA | 2-[2-(2-Bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrobromide | C ₁₇ H ₁₇ BrN ₂ S HBr | 360.03 | 361.0 (rel. int.= 96) | 177-179 |
| P | 2-[2-(3-Iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; hydrobromide | C ₁₇ H ₁₇ IN ₂ S HBr | 408.02 | 409 | 183-185 |
| AG | 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole; hydrobromide | C ₂₁ H ₂₃ N ₃ O ₃ S HBr | 397.15 | 398.1 | >240 |
| AL | 2-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; hydrochloride | C ₂₂ H ₂₂ N ₂ OS HCl | 362.1 | 363 | |
| AM | 2-[2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; hydrochloride | C ₁₈ H ₁₉ BrN ₂ OS HCl | 390 | 390.9 | |

Example 2: Scincillation Proximity Assay (SPA)

High-Throughput Receptor Binding Screening for MC4-R Binding Compounds

A. Preparation of Membranes from MC4-R Cells

5 A crude preparation of plasma membranes, of sufficient purity for use in the scincillation proximity assay (SPA), was prepared using the following protocol (Maeda et al. (1983) *Biochem. Biophys. Acta* 731:115-120).

MC4-R cells were stable recombinant K293 cells overexpressing the MC4-R. The cells were routinely cultured and passaged in a growth medium composed of
10 DMEM base medium: 10% fetal bovine serum (FBS), 1X Glutamine, and 0.5 mg/ml G418. Terminal cultures (i.e., those which will be processed to produce plasma membranes) were grown in identical media, with the exception that the media contained 0.2 mg/ml G418.

At 4°C, harvested cells were pelleted and immediately washed with 25 mL of
15 PBS. The washed cells were resuspended in two volumes of STM buffer (0.25 M sucrose, 5 mM Tris, 1 mM MgCl₂, pH 7.5), containing Boehringer CompleteTM protease inhibitors. Cell breakage was accomplished using a Dounce homogenizer. After 20-30 strokes, nuclei and unbroken cells were pelleted by centrifugation at 1100 rpm for 5 minutes. The supernatant was saved and the pellet was resuspended in 1 volume of
20 STM/protease inhibitors, and then a further lysis step was carried out by the Dounce homogenizer (10-20 strokes). This material was then combined with the first supernatant. 11.25 mL of the homogenate was gently layered on top of 27.25 mL of 42% (w/w) sucrose (5 mM Tris, 1 mM MgCl₂, pH 7.5). After spinning at 28,000 rpm (ultracentrifuge, SW-28 rotor) for 90 minutes, membranes were collected at the interface
25 with a transfer pipette.

The membrane suspension obtained from the sucrose interface was collected and diluted with 5 mM Tris and 1 mM MgCl₂. Membranes were collected by a further round of centrifugation at 33,000 rpm for 30 minutes (SW-41 Ti rotor). The pellet of membranes was subsequently resuspended in a small (0.5 mL) volume of STM, using a
30 2 mL Dounce homogenizer, and immediately frozen. The resulting membranes were stable to both freeze-thaw cycles and temperatures around 4°C for at least 6 hours.

B. High-throughput screen

A scincillation proximity assay (SPA) format ligand binding assay was used.
35 The membranes from the MC4-R mammalian cells (K293 expressing MC4-R) were bound to wheat germ agglutinin (WGA) coated SPA beads. The membrane coated SPA beads were added to screening plates, which contained the test compounds pre-dissolved in 30µL of 10% DMSO. After pre-equilibration of the receptor coated beads with the

test compounds (1 hour), 2nM of radioactive ligand ($[^{125}\text{I}]\text{NDP-}\alpha\text{-MSH}$) was added. Since the binding of the radioactive ligand to the receptor causes the scintillation of the beads, blockage of the binding of the radioactive ligand by a small molecule causes a reduction in scintillation.

5

1. Pre-Binding of the MC4R Membranes to the WGA-SPA beads

The membranes were mixed with the SPA beads to make a 2X stock of membrane and beads.

For a twenty plate batch of screening plates, the components were mixed in proportions given in Table 2. The membranes and beads were stirred with a magnetic stir bar at room temperature for 1-2 hours to allow binding.

Table 2

| Component | Volume | Final Concentration in Assay |
|------------------------------|---------------------|------------------------------|
| 4 mg/ml WGA-SPA Beads | 14.4 mL | 25 $\mu\text{g}/\text{well}$ |
| MC4R crude plasma membranes* | 600 μL * | 5 $\mu\text{g}/\text{well}$ |
| SPA Binding Buffer | 100 mL | N/A |

15 * the exact amount of membranes used varies with the quality of the membrane preparation and must be checked for each new batch.

2. Binding Assay

The following assay was performed with automation using a Titertec MultiDrop with plate stacker.

20 30 μL of 10% DMSO was added per well to the dried compound film in an OptiPlate. Then, 5 μL of cold NDP- α -MSH was added to the control wells. Subsequently, 50 μL per well of 2X membranes and beads were added and pre-equilibrated with the compounds for 1 hour.

Binding was initiated by adding 20 μL of radioactive ligand (a 20 nM solution of $[^{125}\text{I}]\text{-NDP-}\alpha\text{-MSH}$) to each test well. The plates were incubated overnight at room temperature and read the following morning.

25 The reagents and amounts are summarized below in Table 3.

Table 3

| Reagent | Volume (μL) | | | |
|---|-------------|----------|-----|------|
| | Max (100%) | Min (0%) | 50% | Test |
| 20% DMSO | 30 | 30 | 30 | 30 |
| 2X membranes + beads | 60 | 0 | 60 | 60 |
| 2nM [¹²⁵ I]-NDP-α-MSH in binding buffer | 20 | 20 | 20 | 20 |
| NDP-α-MSH (5μM in H ₂ O) | 5 | 0 | 0 | 0 |
| NDP-α-MSH (20 nM in H ₂ O) | 0 | 0 | 5 | 0 |
| Test Compound* | 0 | 0 | 0 | 5μM |

* Test compound stock diluted in BuOH 1:10, 25 μL dried in assay plate in hood prior to addition of assay buffer. Well contained

5 0.5 nmol of each test compound (20/well) in 2.5 μL 100% DMSO.

Potency of inhibitors was quantified with respect to positive (100% inhibition) and negative (no inhibitor; 0% inhibition) controls. The following formula was used:

10
$$\% \text{ Inhibition} = \{1 - [\text{cpm} - (\text{positive control})] / [(\text{negative control}) - (\text{positive control})]\} * 100\%$$

Results from the SPA, are summarized in Table 4. In Table 4, * indicates good inhibition of the MC4-R, ** indicates very good inhibition of the MC4-R, and *** indicates exemplary inhibition of the MC4-R.

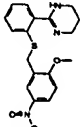
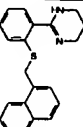
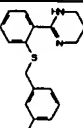
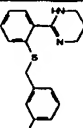
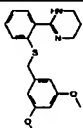
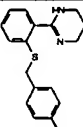
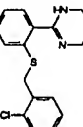
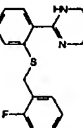
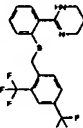
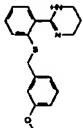
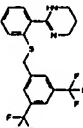
15 Compounds which were found to be not active as MC4-R binding compounds, using the SPA assay described herein, are depicted in Table 5.

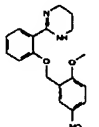
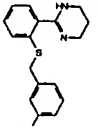
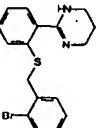
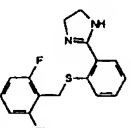
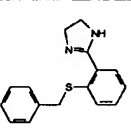
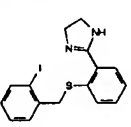
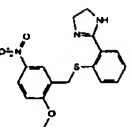
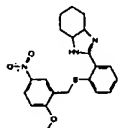
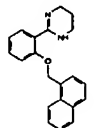
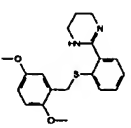
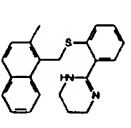
In an embodiment, the present invention pertains to the compounds and methods described herein provided that the compound is not selected from the group consisting of those depicted in Table 5.

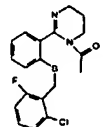
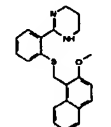
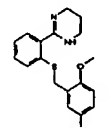
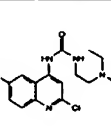
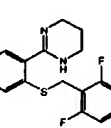
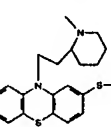
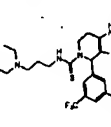
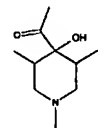
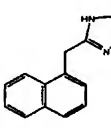
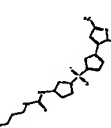
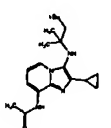
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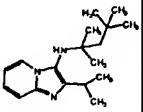
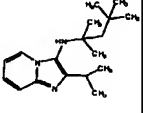
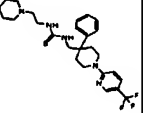
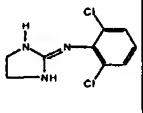
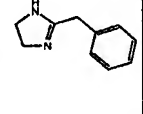
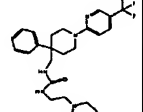
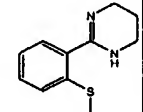
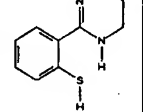
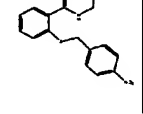
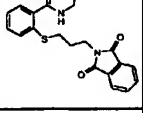
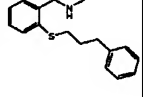
Table 4

| ID | CHEMICAL NAME | Mol Weight (Tot) | Structure | MC4-R Binding |
|----|--|------------------|-----------|---------------|
| A | 2-[2-(2,5-Dichlorothiophen-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 393.7877 | | ** |
| B | 2-[2-(2-Chloro-6-fluorobenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 415.7566 | | ** |
| D | 2-(2-Benzylsulfanyl-phenyl)-1,4,5,6-tetrahydropyrimidine; HBr | 363.3214 | | * |
| E | 2-(2-Pentadecylsulfanyl-phenyl)-1,4,5,6-tetrahydropyrimidine; HBr | 483.6 | | * |
| F | 2-(2-Cyclohexylmethylsulfanyl-phenyl)-1,4,5,6-tetrahydropyrimidine; HBr | 369.369 | | * |
| G | 2-[2-(2-Methylbenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 377.3483 | | * |
| H | 2-[2-(3-Nitrobenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 408.319 | | * |
| I | 2-[2-(4-Benzoyloxybenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 424.9934 | | ** |
| M | 2-[2-(2-Iodobenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 444.7659 | | ** |

| | | | | |
|---|--|----------|---|-----|
| N | 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 438.3453 |  | *** |
| O | 2-[2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 368.9293 |  | *** |
| P | 2-[2-(3-Iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 489.2179 |  | ** |
| Q | 2-[2-(3-Chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine | 397.7662 |  | * |
| R | 2-[2-(3,5-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 378.922 |  | ** |
| S | 2-[2-(4-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 381.3119 |  | * |
| T | 2-[2-(2-Chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine | 397.7662 |  | * |
| U | 2-[2-(2-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 381.3119 |  | * |
| V | 2-[2-(2,4-Bis(trifluoromethyl)-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 499.3179 |  | * |
| W | 2-[2-(3-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 348.8957 |  | * |
| X | 2-[2-(3,5-Bis(trifluoromethyl)-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 454.8659 |  | * |

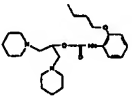
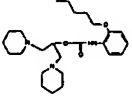
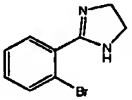
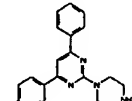
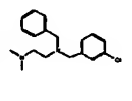
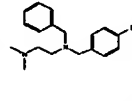
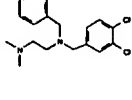
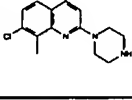
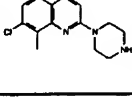
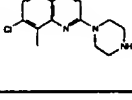
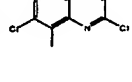
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|----|--|----------|---|-----|
| Y | 2-[2-(2-Methoxy-5-nitro-benzoyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 377.8267 |  | ** |
| Z | 2-[2-(3-Bromo-benzoyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 442.2175 |  | ** |
| AA | 2-[2-(2-Bromo-benzoyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 442.2175 |  | ** |
| AB | 2-[2-(2-Chloro-6-fluoro-benzoyl)-phenyl]-4,5-dihydro-1H-imidazole | 357.2777 |  | * |
| AC | 2-(2-Benzoylsulfonyl-phenyl)-4,5-dihydro-1H-imidazole; HCl | 304.8425 |  | * |
| AE | 2-[2-(2-Iodo-benzoyl)-phenyl]-4,5-dihydro-1H-imidazole; HCl | 430.7391 |  | ** |
| AF | 2-[2-(2-Methoxy-5-nitro-benzoyl)-phenyl]-4,5-dihydro-1H-imidazole; HBr | 424.3184 |  | ** |
| AG | 2-[2-(2-Methoxy-5-nitro-benzoyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzotriimidazole; HBr | 478.41 |  | *** |
| AH | 2-[2-(Naphthalen-1-ylmethoxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 362.4327 |  | ** |
| AI | 2-[2-(2,5-Dimethoxy-benzoyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 378.922 |  | ** |
| AJ | 2-[2-(2-Methyl-naphthalen-1-ylmethoxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 346.4962 |  | *** |

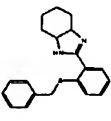
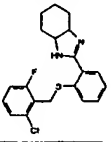
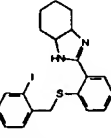
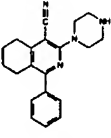
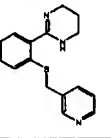
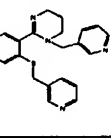
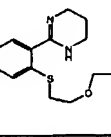
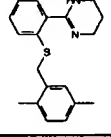
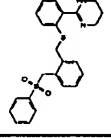
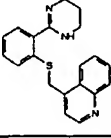
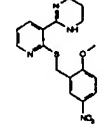
| | | | | |
|----|--|----------|---|-----|
| AK | 1-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone | 376.8819 |  | ** |
| AL | 2-[2-(2-Methoxynaphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 398.9556 |  | *** |
| AM | 2-[2-(5-Bromo-2-methoxybenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 427.7917 |  | *** |
| AN | 1-(6-Bromo-2-chloro-quinolin-4-yl)-3-[2-(diethylaminoethyl)-urea | 399.7179 |  | * |
| AO | 2-[2-(2,6-Difluorobenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 480.2143 |  | * |
| AP | 10-[2-(1-Methylpiperidin-2-yl)-ethyl]-2-methylsulfanyl-10H-phenothiazine; HCl | 407.0429 |  | * |
| AQ | 4-(3,5-Bis(trifluoromethyl)-phenyl)-1,4,6,7-tetrahydroimidazo[4,5-c]pyridine-5-carboxylic acid (3-diethylamino-propyl)-amide | 507.5465 |  | * |
| AR | 1-(4-Hydroxy-1,3,5-trimethylpiperidin-4-yl)-ethanone | 185.2664 |  | ** |
| AS | 2-Naphthalen-1-ylmethyl-4,5-dihydro-1H-imidazole; HCl | 246.7386 |  | * |
| AT | 1-(3-Diethylamino-propyl)-3-[1-[5-(2-methyl-5-trifluoromethyl-2H-pyrazol-3-yl)-thiophen-2-ylthio]pyrrolidin-2-yl]-thiourea | 552.7096 |  | * |
| AU | N-[2-Cyclopropyl-3-(1,1,3,3-tetramethylbutylamino)-imidazo[1,2-a]pyridin-8-yl]-acetamide | 342.4846 |  | * |

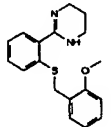
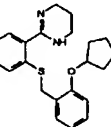
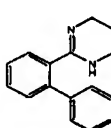
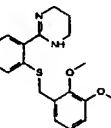
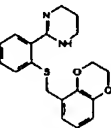
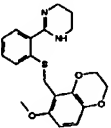
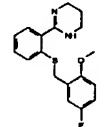
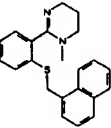
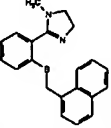
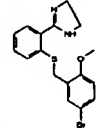
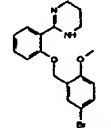
| | | | | |
|----|--|----------|---|---|
| AV | (2-Isopropyl-imidazo[1,2-a]pyridin-3-yl)-(1,1,3,3-tetramethyl-butyl)amine | 342.4846 |  | * |
| AW | (2-Isopropyl-imidazo[1,2-a]pyridin-3-yl)-(1,1,3,3-tetramethyl-butyl)amine | 287.4485 |  | * |
| AX | 1-(4-Phenyl-5'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2]bipyridin-4-ylmethyl)-3-(2-piperidin-1-ylethyl)-urea | 505.6509 |  | * |
| AY | (2,6-Dichlorophenyl)-imidazolidin-2-ylidene-amine; HCl | 266.5561 |  | * |
| AZ | 2-Benzyl-4,5-dihydro-1H-imidazole | 160.2188 |  | * |
| BA | 1-(4-Phenyl-5'-trifluoromethyl-3,4,5,6-tetrahydro-2H-[1,2]bipyridin-4-ylmethyl)-3-(2-piperidin-1-ylethyl)-urea | 489.5843 |  | * |
| BB | 2-(2-Methylsulfanylphenyl)-1,4,5,6-tetrahydropyrimidine | 334.2216 |  | * |
| BZ | 2-(1,4,5,6-Tetrahydropyrimidin-2-yl)-benzenethiol | 192.2848 |  | * |
| BD | 2-(2-(4-Nitrobenzylsulfanyl)phenyl)-1,4,5,6-tetrahydropyrimidine | 408.319 |  | * |
| BE | 2-(3-(2-(1,4,5,6-Tetrahydropyrimidin-2-yl)phenylsulfanyl)propyl)-isindole-1,3-dione; HBr | 460.3948 |  | * |
| BF | 2-(2-(3-Phenylpropylsulfanyl)phenyl)-1,4,5,6-tetrahydropyrimidine; HBr | 391.3752 |  | * |

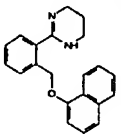
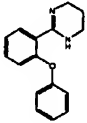
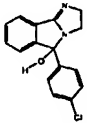
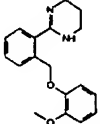
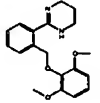
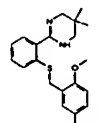
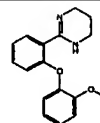
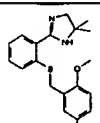
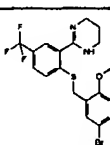
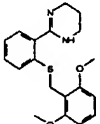
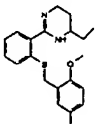
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|----|---|----------|--|---|
| BG | 2-[2-(4-Trifluoromethylbenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 431.3197 | | * |
| BH | 4-Piperazin-1-yl-2-trifluoromethylquinoline | 281.2806 | | * |
| BI | 3-Nitrobenzamide; HCl | 201.6116 | | * |
| BJ | 4-Carbamidoylbenzamide | 163.1791 | | * |
| BK | 2-Phenyl-4,5-dihydro-1H-imidazole | 146.1919 | | * |
| BL | 2-(3-Benzylsulfanylphenyl)-1,4,5,6-tetrahydropyrimidine | 282.4094 | | * |
| BM | 2-[2-(4-tert-Butylbenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 419.4289 | | * |
| BN | 2,2-Diphenyl-4-[2-(1,4,5,6-tetrahydropyrimidin-2-yl)phenylsulfanyl]butyronitrile; HBr | 492.4827 | | * |
| BO | 2-[2-(3,4-Dimethylbenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 346.9232 | | * |
| BQ | 3-[2-(1,4,5,6-Tetrahydropyrimidin-2-yl)phenylsulfanyl]benzonitrile; HBr | 388.3312 | | * |
| BR | 2-[2-(4-Bromobenzylsulfanyl)phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 442.2175 | | * |

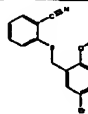
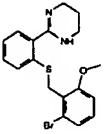
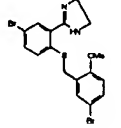
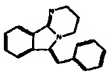
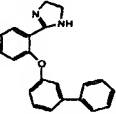
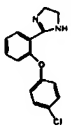
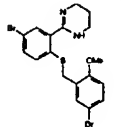
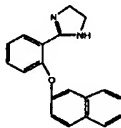
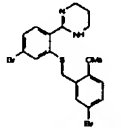
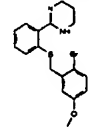
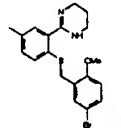
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|----|--|----------|--|---|
| BS | 2-[2-(2,6-Dichloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 432.2109 | | * |
| BT | 2-[2-(Naphthalen-2-ylmethanesulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 413.3813 | | * |
| BU | 2-[2-(4-Fluorobenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 381.3119 | | * |
| BV | 2-[2-(Biphenyl-4-ylmethanesulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 394.9672 | | * |
| BW | 2-[2-(2,4-Bis(trifluoromethyl)-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 499.3179 | | * |
| BX | 2-[2-(1,4,5,6-Tetrahydropyrimidin-2-yl)-phenylsulfanylmethyl]-benzonitrile; HBr | 388.3312 | | * |
| BY | 4-[2-(1,4,5,6-Tetrahydropyrimidin-2-yl)-phenylsulfanylmethyl]-benzonitrile; HBr | 388.3312 | | * |
| BZ | 2-[2-(4-Methoxybenzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 348.8957 | | * |
| CA | Benzamidine; HCl | 156.614 | | * |
| CB | 3,5-Bis(trifluoromethyl)-benzamidine; HCl | 292.6105 | | * |
| CC | 2-[2-Benzylsulfanyl-phenyl]-4,5-dihydro-1H-imidazole; HCl | 304.8425 | | * |

| | | | | |
|----|--|----------|---|----|
| CD | (2-Butoxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-ylmethylethyl ester; Formate | 463.6221 |  | .. |
| CE | (2-Pentyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-ylmethylethyl ester; Formate | 477.649 |  | .. |
| CF | 2-(2-Bromo-phenyl)-4,5-dihydro-1H-imidazole; HCl | 261.5479 |  | * |
| CJ | 4-Phenyl-2-piperazin-1-yl-6-p-tolyl-pyrimidine | 330.4326 |  | * |
| CK | N-Benzyl-N-(3-chloro-benzyl)-N',N'-dimethylethane-1,2-diamine | 302.8468 |  | * |
| CL | N-Benzyl-N-(4-bromo-benzyl)-N',N'-dimethylethane-1,2-diamine | 347.2981 |  | * |
| CM | N-Benzyl-N-(3,4-dichloro-benzyl)-N',N'-dimethylethane-1,2-diamine | 337.2916 |  | * |
| CO | 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline; Oxalate | 365.8208 |  | * |
| CP | 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline | 275.7808 |  | * |
| CQ | 7-Chloro-4,8-dimethyl-2-piperazin-1-yl-quinoline; Formate | 321.8108 |  | * |
| CS | 2,7-Dichloro-4,8-dimethyl-quinoline | 226.1046 |  | * |

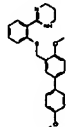
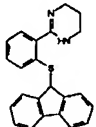
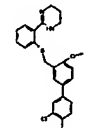
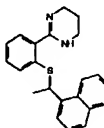
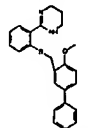
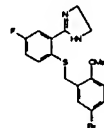
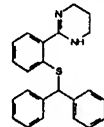
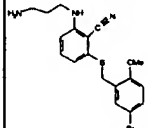
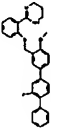
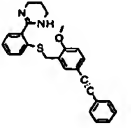
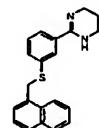
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|----|---|----------|---|----|
| CT | 2-{2-(2-Benzylsulfanyl-phenyl)-3a,4,5,6,7,7a-hexahydro-1H-benzimidazole; HCl | 358.9342 |  | * |
| CU | 2-{2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl}-3a,4,5,6,7,7a-hexahydro-1H-benzimidazole; HCl | 411.3694 |  | ** |
| CV | 2-{2-(2-Iodo-benzylsulfanyl)-phenyl}-3a,4,5,6,7,7a-hexahydro-1H-benzimidazole; HCl | 484.8307 |  | ** |
| CY | 1-Phenyl-3-piperazin-1-yl-5,8,7,8-tetrahydroisoquinoline-4-carbonitrile | 318.4216 |  | ** |
| CZ | 2-{2-(Pyridin-3-ylmethylsulfanyl)-phenyl}-1,4,5,6-tetrahydro-pyrimidine | 283.3972 |  | * |
| DA | 1-Pyridin-3-ylmethyl-2-{2-(pyridin-3-ylmethylsulfanyl)-phenyl}-1,4,5,6-tetrahydro-pyrimidine | 374.5096 |  | * |
| DB | 2-{2-(2-Ethoxyethylsulfanyl)-phenyl}-1,4,5,6-tetrahydro-pyrimidine; HBr | 345.3037 |  | * |
| DC | 2-{2-(2,5-Dimethylbenzylsulfanyl)-phenyl}-1,4,5,6-tetrahydro-pyrimidine; HCl | 346.9232 |  | ** |
| DD | 2-{2-(2-Benzenesulfonylmethyl-benzylsulfanyl)-phenyl}-1,4,5,6-tetrahydro-pyrimidine; HBr | 517.5108 |  | * |
| DE | 4-{2-[1,4,5,6-Tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-quinoline; HBr | 414.3691 |  | ** |
| DF | 2-{2-(2-Methoxy-5-nitro-benzylsulfanyl)-pyridin-3-yl}-1,4,5,6-tetrahydro-pyrimidine; HBr | 439.3331 |  | ** |

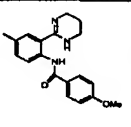
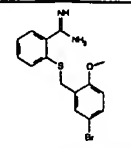
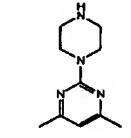
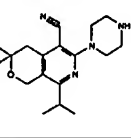
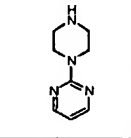
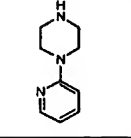
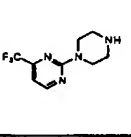
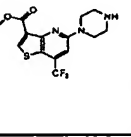
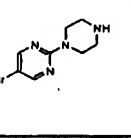
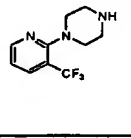
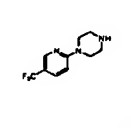
| | | | | |
|----|--|----------|---|-----|
| DG | 2-[2-(2-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 348.8957 |  | ** |
| DH | 2-[2-(2-Cyclopentylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 447.4393 |  | ** |
| DI | 2-Biphenyl-2-yl-1,4,5,6-tetrahydro-pyrimidine; Formate | 282.3465 |  | * |
| DJ | 2-[2-(2,3-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 423.374 |  | * |
| DK | 2-[2-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 421.3581 |  | ** |
| DL | 2-[2-(6-Methoxy-2,3-dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 451.3844 |  | *** |
| DM | 2-[2-(5-fluoro-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole; HCl | 411.3381 |  | ** |
| DN | 1-Methyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; formate | 392.5262 |  | ** |
| DO | 1-Methyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole | 332.4693 |  | *** |
| DP | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole; HCl | 413.7649 |  | *** |
| DQ | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 411.7251 |  | *** |

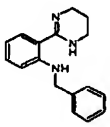
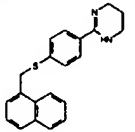
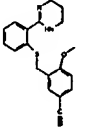
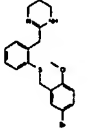
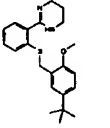
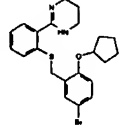
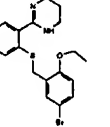
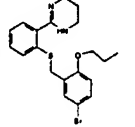
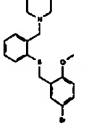
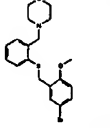
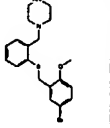
| | | | | |
|----|---|----------|---|-----|
| DR | 2-[2-(Naphthalen-1-yloxy-methyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 316.4027 |  | ** |
| DS | 2-[2-(Phenoxy-phenyl)-1,4,5,6-tetrahydro-pyrimidine; HCl | 288.7759 |  | * |
| DT | 5-(4-Chloro-phenyl)-2,5-dihydro-3H-imidazo[2,1-a]isoindol-5-ol | 284.7448 |  | * |
| DU | 2-[2-(2-Methoxy-phenoxy-methyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 332.8291 |  | * |
| DV | 2-[2-(2,6-Dimethoxy-phenoxy-methyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 326.3954 |  | * |
| DW | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine | 419.3855 |  | *** |
| DX | 2-[2-(2-Methoxy-phenoxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 328.3722 |  | * |
| DY | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole | 405.3586 |  | *** |
| DZ | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 459.33 |  | * |
| EA | 2-[2-(2,6-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 378.922 |  | *** |
| EB | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-pyrimidine | 419.3855 |  | *** |

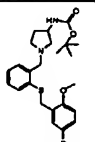
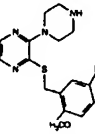
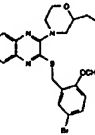
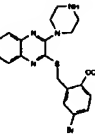
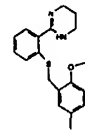
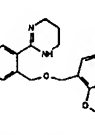
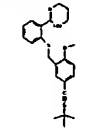
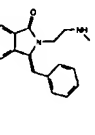
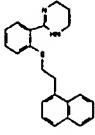
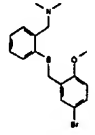
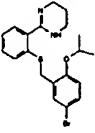
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|----|--|----------|---|-----|
| EC | 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzonitrile | 334.2364 |  | * |
| ED | 2-[2-(2-Bromo-6-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 472.2437 |  | *** |
| EF | 2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole; Formate | 502.2309 |  | *** |
| EJ | 9-Benzylidono-1,2,3,9-tetrahydro-4,9a-diaza-fluorene; Formate | 306.3685 |  | * |
| EK | 2-[2-(Biphenyl-3-yl-oxo)-phenyl]-4,5-dihydro-1H-imidazole | 314.3868 |  | * |
| EL | 2-[2-(4-Chlorophenoxy)-phenyl]-4,5-dihydro-1H-imidazole | 272.7338 |  | * |
| EM | 2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 516.2578 |  | *** |
| EN | 2-[2-(Naphthalen-2-yl-oxo)-phenyl]-4,5-dihydro-1H-imidazole; Formate | 334.3789 |  | * |
| EO | 2-[4-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 470.2278 |  | ** |
| EP | 2-[2-(2-Bromo-5-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 472.2437 |  | *** |
| EQ | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 405.3586 |  | *** |

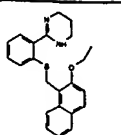
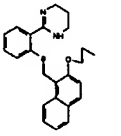
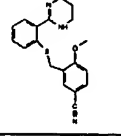
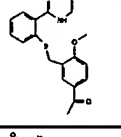
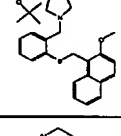
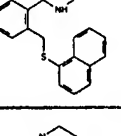
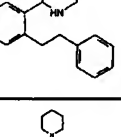
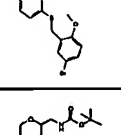
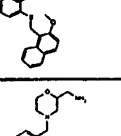
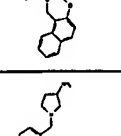
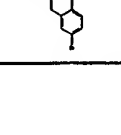
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|----|--|----------|--|-----|
| ER | 2-[2-(Naphthalen-1-yloxy)-phenyl]-4,5-dihydro-1H-imidazole; Formate | 334.3789 | | * |
| ES | 2-[2-(Naphthalen-1-yloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 348.4058 | | * |
| ET | 2-[2-(Biphenyl-3-ylmethanesulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 439.4192 | | ** |
| EU | 2-[2-(Naphthalen-2-yloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 348.4058 | | * |
| EV | 2-[2-(5-Bromo-2-methoxy-phenylmethanesulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 407.3311 | | * |
| EW | 2-[2-(5-Chloro-2-methoxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 383.3404 | | *** |
| EX | 2-[2-(2-Methoxy-5-thiophen-3-yl-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 431.0216 | | *** |
| EY | 2-[2-(Biphenyl-2-ylmethanesulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 404.5372 | | ** |
| EZ | 2-[2-(5-Iodo-2-methoxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 484.3622 | | *** |
| FA | 2-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-5-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 409.3222 | | *** |
| FB | 2-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 409.3222 | | *** |

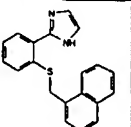
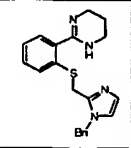
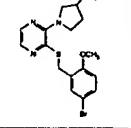
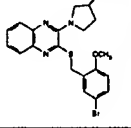
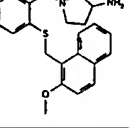
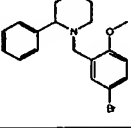
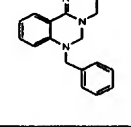
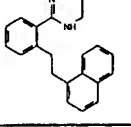
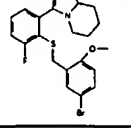
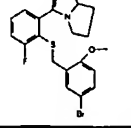
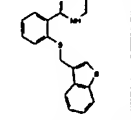
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|----|--|----------|---|-----|
| FC | 2-[2-(4,4'-Dimethoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 499.4717 |  | ** |
| FD | 2-[2-(9H-Fluoren-9-ylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 437.4033 |  | ** |
| FE | 2-[2-(3'-Chloro-4'-fluoro-4-methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 486.9987 |  | ** |
| FF | 2-[2-(1-Naphthalen-1-ylethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 382.9562 |  | *** |
| FG | 2-[2-(4-Methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 434.5634 |  | *** |
| FH | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-4,5-dihydro-1H-imidazole; Formate | 441.3253 |  | *** |
| FI | 2-[2-Benzhydrylsulfanyl-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 404.5372 |  | *** |
| FJ | 2-(3-Amino-propylamino)-6-(5-bromo-2-methoxybenzylsulfanyl)-benzonitrile; Formate | 452.3764 |  | * |
| FK | 2-[2-(2'-Fluoro-4'-methoxy-[1,1':4',1'']terphenyl-3'-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 528.6517 |  | ** |
| FL | 2-[2-(2-Methoxy-5-phenylsulfanyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 458.5854 |  | ** |
| FM | 2-[3-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 378.4993 |  | * |

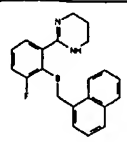
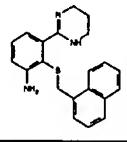
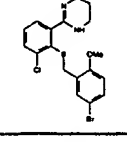
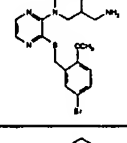
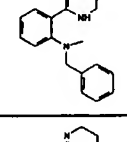
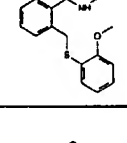
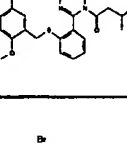
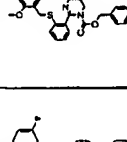
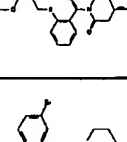
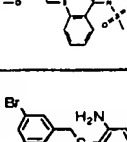
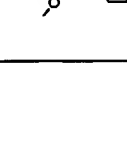
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|----|---|----------|---|----|
| FN | 4-Methoxy-N-(4-methyl-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl)-benzamide; Formate | 369.4248 |  | * |
| FO | 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzamidine; formate | 397.297 |  | ** |
| FP | 4,8-Dimethyl-2-piperazin-1-yl-pyrimidine | 192.264 |  | * |
| FQ | 8-Isopropyl-3,3-dimethyl-6-piperazin-1-yl-3,4-dihydro-1H-pyrano[3,4-c]pyridine-5-carbonitrile | 314.4308 |  | * |
| FR | 2-Piperazin-1-yl-pyrimidine | 164.2102 |  | * |
| FS | 1-Pyridin-2-yl-piperazine | 163.2224 |  | * |
| FT | 2-Piperazin-1-yl-4-trifluoromethyl-pyrimidine | 232.2085 |  | * |
| FU | 5-Piperazin-1-yl-7-trifluoromethyl-thieno[3,2-b]pyridine-3-carboxylic acid methyl ester | 345.3454 |  | * |
| FV | 5-Bromo-2-piperazin-1-yl-pyrimidine | 243.1063 |  | * |
| FW | 1-(3-Trifluoromethyl-pyridin-2-yl)-piperazine | 231.2207 |  | * |
| FX | 1-(5-Trifluoromethyl-pyridin-2-yl)-piperazine | 231.2207 |  | * |

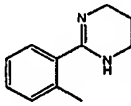
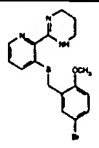
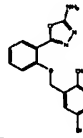
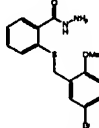
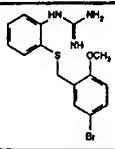
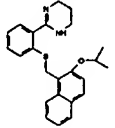
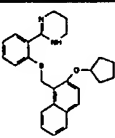
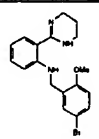
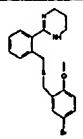
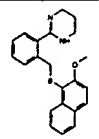
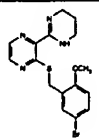
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|----|---|----------|---|-----|
| FY | Benzyl-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl-amine | 265.3581 |  | * |
| FZ | 2-[4-(Naphthalen-1-ylmethanesulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 378.4993 |  | ** |
| GA | 2-[2-(5-Ethynyl-2-methoxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 372.9177 |  | *** |
| GB | 2-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 441.8186 |  | ** |
| GC | 2-[2-(5-tert-Butyl-2-methoxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 405.0032 |  | * |
| GD | 2-[2-(5-Bromo-2-cyclopentyloxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 491.4534 |  | *** |
| GE | 2-[2-(5-Bromo-2-ethoxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 441.8186 |  | *** |
| GF | 2-[2-(5-Bromo-2-propoxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 455.8455 |  | *** |
| GG | [2-(5-Bromo-2-methoxy-benzylsulfonyl)-benzyl]-diethyl-amine; HCl | 430.8357 |  | ** |
| GH | 4-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-benzyl]-morpholine; HCl | 444.8192 |  | * |
| GI | 1-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-benzyl]-piperazine; Oxalate | 497.4145 |  | ** |

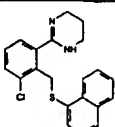
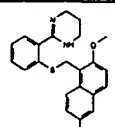
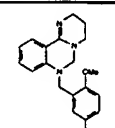
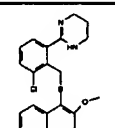
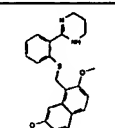
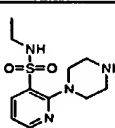
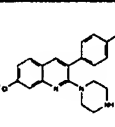
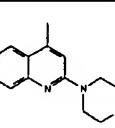
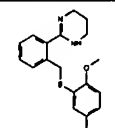
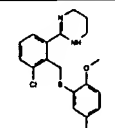
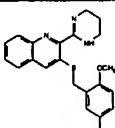
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|----|--|----------|---|-----|
| GK | (1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-yl)-carbamic acid tert-butyl ester | 507.4918 |  | * |
| GL | 3'-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2]bipyrazinyl | 395.3232 |  | * |
| GM | C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-morpholin-2-yl}-methylamine; 2HCl | 548.3308 |  | ** |
| GN | 2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-piperazin-1-yl-quinoxaline; Formate | 491.4131 |  | * |
| GO | 2-[2-(2-Methoxy-5-methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 362.9226 |  | *** |
| GP | 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 425.752 |  | *** |
| GQ | 2-[2-[5-(3,3-Dimethyl-but-1-ynyl)-2-methoxy-benzylsulfanyl]-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 429.0252 |  | * |
| GR | 3-Benzylidene-2-(2-methylamino-ethyl)-2,3-dihydro isoindol-1-one | 278.3538 |  | * |
| GS | 2-[2-(2-Naphthalen-1-ylethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 346.4962 |  | * |
| GU | [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-dimethylamine; HCl | 402.7819 |  | ** |
| GV | 2-[2-(5-Bromo-2-isopropoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 455.8455 |  | *** |

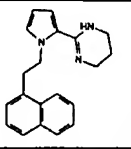
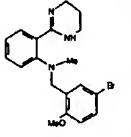
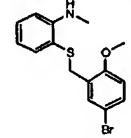
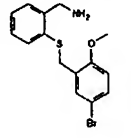
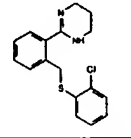
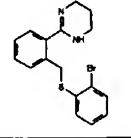
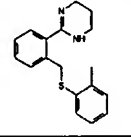
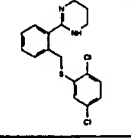
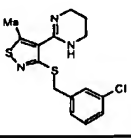
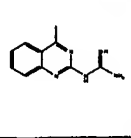
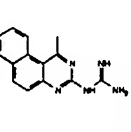
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|----|--|----------|---|-----|
| GW | 2-[2-(2-Ethoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 412.9824 |  | *** |
| GX | 2-[2-(2-Propoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 427.0093 |  | *** |
| GY | 4-Methoxy-3-[2-(1,4,5,6-tetrahydropyrimidin-2-yl)-phenylsulfanylmethyl]-benzonitrile; HCl | 373.9055 |  | *** |
| GZ | 1-[4-Methoxy-3-[2-(1,4,5,6-tetrahydropyrimidin-2-yl)-phenylsulfanylmethyl]-phenyl]-ethanone; Formate | 400.503 |  | ** |
| HA | [1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-yl]-carbamic acid tert-butyl ester | 478.6556 |  | * |
| HB | 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 368.9293 |  | *** |
| HC | 2-[2-Phenethyl-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 310.4003 |  | * |
| HD | 1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzyl]-piperidine; Formate | 452.4167 |  | ** |
| HE | [4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-ylmethyl]-carbamic acid tert-butyl ester | 508.6819 |  | * |
| HF | C-[4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl]-methylamine; 2HCl | 481.486 |  | ** |
| HG | 1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzyl]-pyrrolidin-3-ylamine; 2HCl | 480.2959 |  | ** |

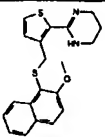
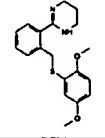
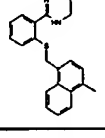
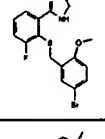
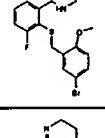
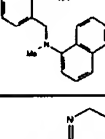
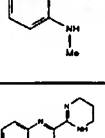
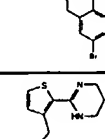
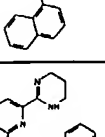
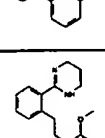

| | | | | |
|----|---|----------|---|-----|
| HH | 2-[2-(Naphthalen-1-ylmethanesulfonyl)-phenyl]-1H-imidazole | 316.4265 |  | * |
| HI | 2-[2-(1-Benzyl-1H-imidazol-2-ylmethanesulfonyl)-phenyl]-1,4,5,6-tetrahydropyrimidine | 362.4986 |  | * |
| HJ | 1-[3-(5-Bromo-2-methoxybenzylsulfonyl)-pyrazin-2-yl]-pyrrolidin-3-ylamine; 2HCl | 468.2446 |  | * |
| HK | 1-[3-(5-Bromo-2-methoxybenzylsulfonyl)-quinoxalin-2-yl]-pyrrolidin-3-ylamine; 2HCl | 518.3045 |  | * |
| HL | 1-[2-(2-Methoxynaphthalen-1-ylmethanesulfonyl)-benzyl]-pyrrolidin-3-ylamine; HCl | 414.9983 |  | ** |
| HM | 1-(5-Bromo-2-methoxybenzyl)-2-phenylpiperidine | 360.2938 |  | * |
| HN | 9-Benzyl-2,3,8,10-tetrahydro-1H-4,9,10a-triazaphenanthrene; Formate | 323.3991 |  | * |
| HO | 2-[2-(2-Naphthalen-1-ylethyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; Formate | 360.4602 |  | *** |
| HP | 3-[2-(5-Bromo-2-methoxybenzylsulfonyl)-3-fluoro-phenyl]-1,5,6,7,8,8a-hexahydroimidazo[1,5-a]pyridine; HCl | 485.847 |  | *** |
| HQ | 3-[2-(5-Bromo-2-methoxybenzylsulfonyl)-3-fluoro-phenyl]-5,6,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole; Formate | 481.3901 |  | *** |
| HR | 2-[2-(Benzo[b]thiophen-3-ylmethanesulfonyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HBr | 419.4094 |  | *** |

| | | | | |
|----|--|----------|---|-----|
| HS | 2-[3-Fluoro-2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 396.4897 |  | *** |
| HT | 2-(Naphthalen-1-ylmethylsulfanyl)-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine; Formate | 393.514 |  | ** |
| HU | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 471.8065 |  | *** |
| HV | C-44-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-morpholin-2-yl)-methylamine; Formate | 471.3795 |  | * |
| HW | Benzyl-methyl-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl)-amine; Formate | 325.415 |  | * |
| HX | 2-[2-(2-Methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 348.8957 |  | ** |
| HY | 1-[2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl]-3-methyl-butan-1-one | 475.4497 |  | ** |
| HZ | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid benzyl | 525.4662 |  | ** |
| IA | 1-[2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl]-2-phenyl-ethanone | 509.4668 |  | *** |
| IB | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-1-methanesulfonyl-1,4,5,6-tetrahydro-pyrimidine | 469.4234 |  | * |
| IC | 2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenylamine | 324.2413 |  | * |

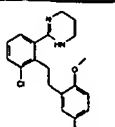
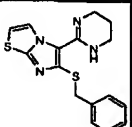
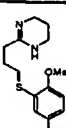
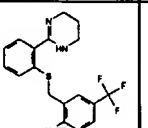
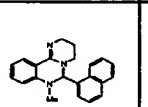
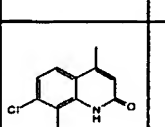
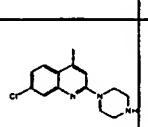
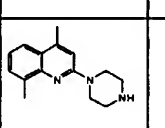
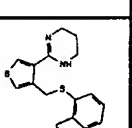
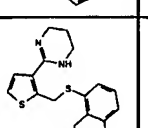
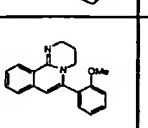
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|----|--|----------|---|-----|
| ID | 2-o-Tolyl-1,4,5,6-tetrahydro-pyrimidine | 174.2456 |  | * |
| IE | 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyridin-2-yl]-1,4,5,6-tetrahydro-pyrimidine | 392.3195 |  | *** |
| IF | 5-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-[1,3,4]oxadiazol-2-ylamine | 392.2762 |  | * |
| IJ | 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzoic acid hydrazide | 367.2664 |  | * |
| IK | N-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-guanidine | 366.2817 |  | ** |
| IL | 2-[2-(2-Isopropoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 436.5793 |  | ** |
| IM | 2-[2-(2-Cyclopentyloxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 453.0472 |  | ** |
| IN | (5-Bromo-2-methoxy-benzyl)-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine | 374.2804 |  | ** |
| IO | 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 451.3886 |  | *** |
| IP | 2-[2-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 398.9556 |  | *** |
| IQ | 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-1,4,5,6-tetrahydro-pyrimidine | 393.3073 |  | ** |

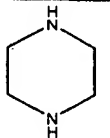
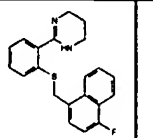
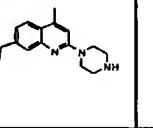
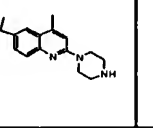
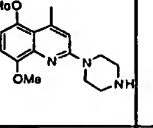
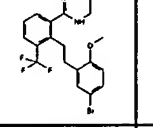
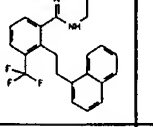
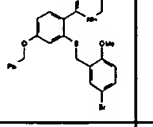
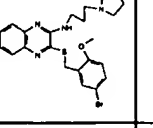
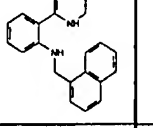
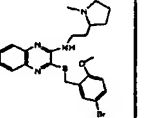
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|----|---|----------|---|-----|
| IR | 2-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 403.374 |  | *** |
| IS | 2-[2-(6-Bromo-2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 477.8516 |  | *** |
| IT | 9-(5-Bromo-2-methoxy-benzyl)-2,3,9,10-tetrahydro-1H-4,9,10a-triaza-phenanthrene; Formate | 432.3214 |  | * |
| IU | 2-[3-Chloro-2-(2-methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 396.9403 |  | *** |
| IV | 2-[2-(2,7-Dimethoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 438.5518 |  | * |
| IW | 2-Piperazin-1-yl-pyridine-3-sulfonic acid ethylamide | 270.3557 |  | * |
| IX | 7-Methoxy-3-(4-nitro-phenyl)-2-piperazin-1-yl-quinoline | 364.404 |  | * |
| IY | 4-Methyl-2-piperazin-1-yl-quinoline | 227.3092 |  | * |
| IZ | 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 427.7917 |  | *** |
| JA | 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 462.2365 |  | *** |
| JB | 3-(5-Bromo-2-methoxy-benzylsulfanyl)-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-quinoline | 442.3794 |  | * |

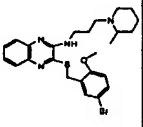
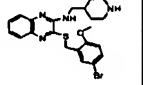
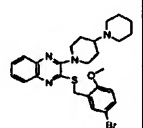
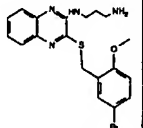
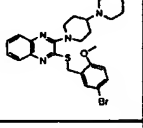
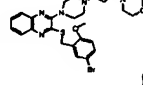
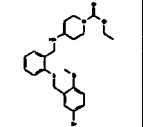
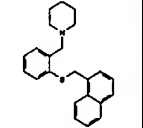
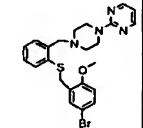
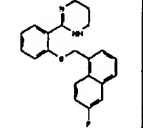
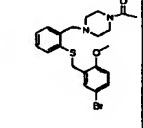
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|----|---|----------|---|-----|
| JC | 2-[1-(2-Naphthalen-1-ylethyl)-1H-pyrol-2-yl]-1,4,5,8-tetrahydropyrimidine | 303.407 |  | ** |
| JD | (5-Bromo-2-methoxy-benzyl-methyl-2-yl)-phenyl-amine | 388.3073 |  | ** |
| JE | [2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-methyl-amine | 338.2682 |  | * |
| JF | 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamine; HCl | 374.7282 |  | ** |
| JK | 2-[2-(2-Chlorophenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 353.3142 |  | ** |
| JL | 2-[2-(2-Bromophenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 397.7655 |  | ** |
| JM | 2-[2-(2-Tolylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 332.8963 |  | ** |
| JN | 2-[2-(2,5-Dichlorophenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydropyrimidine; HCl | 387.7589 |  | *** |
| JO | 2-[3-(3-Chlorobenzylsulfanyl)-5-methyl-isothiazol-4-yl]-1,4,5,6-tetrahydropyrimidine; Formate | 383.927 |  | * |
| JP | N-(4-Methyl-quinazolin-2-yl)-guanidine; HCl | 237.691 |  | * |
| JQ | N-(1-Methyl-benzol[quinoxalin-3-yl]-guanidine; HCl | 287.7509 |  | * |

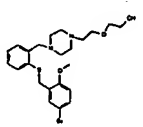
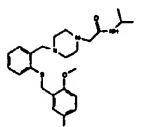
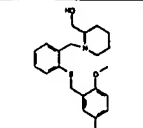
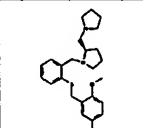
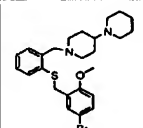
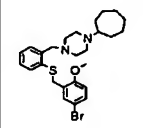
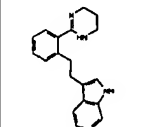
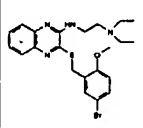
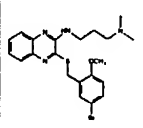
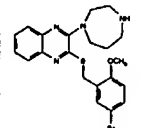
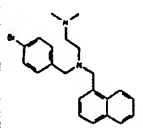
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|----|--|----------|---|-----|
| JR | 2-[3-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 414.5537 |  | ** |
| JS | 2-[2-(2,5-Dimethoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 342.462 |  | ** |
| JT | 2-[2-(4-Methyl-naphthalen-1-ylmethoxy-sulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 382.9562 |  | *** |
| JU | 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-3-fluoro-phenyl]-4,4-dimethyl-1,5-dihydro-1H-imidazole; HCl | 459.8091 |  | *** |
| JV | 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-3-fluoro-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine; HCl | 473.836 |  | *** |
| JW | Methyl-naphthalen-1-yl-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-benzyl]-amine; Formate | 375.4748 |  | * |
| JX | Methyl-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine | 189.2603 |  | * |
| JY | 2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-quinoxaline | 443.3672 |  | * |
| JZ | 2-[3-(Naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 384.5274 |  | *** |
| KA | 2-[6-(2-Naphthalen-1-yl-methoxy)-pyridin-2-yl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 377.4474 |  | * |
| KB | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 373.2926 |  | *** |

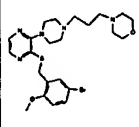
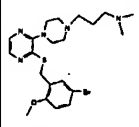
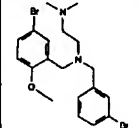
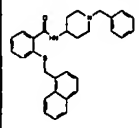
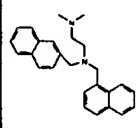
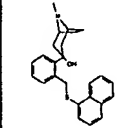
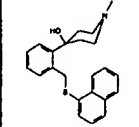
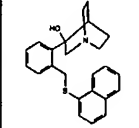
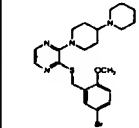
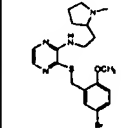
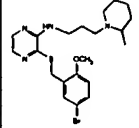
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|----|---|----------|--|-----|
| KC | 10-(5-Bromo-2-methoxy-phenyl)-9-methyl-2,3,9,10-tetrahydro-1H-4,9,10a-triazaphenanthrene; Formate | 432.3214 | | * |
| KD | 2-Morpholin-4-ylmethyl-quinazolin-4-ol | 245.2811 | | * |
| KE | N,N-Dimethyl-N-(4-phenyl-quinazolin-2-yl)-ethane-1,2-diamine | 292.3838 | | * |
| KF | 4-Phenyl-2-piperazin-1-yl-quinazoline | 290.3679 | | * |
| KG | 2-[3-Chloro-2-(2-naphthalen-1-ylethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 385.3349 | | *** |
| KH | 2-[2-(2-(5-Bromo-2-methoxy-phenyl)-ethyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 427.7431 | | *** |
| KI | 1-(2-Naphthalen-1-yl-ethyl)-6-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-1H-pyridin-2-one; Formate | 377.4474 | | * |
| KJ | 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 445.7822 | | *** |
| KK | 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole; HCl | 354.9024 | | *** |
| KL | 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 386.9197 | | *** |
| KM | 2-[3-Bromo-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 447.8253 | | *** |

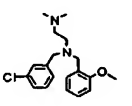
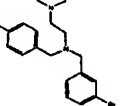
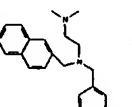
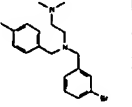
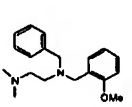
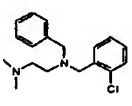
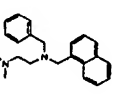
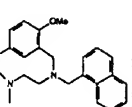
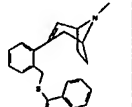
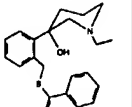
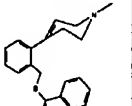
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|----|---|----------|---|-----|
| KN | 2-[2-(2-(5-Bromo-2-methoxy-phenyl)-ethyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 444.1974 |  | *** |
| KO | 6-Benzylsulfanyl-5-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-imidazo[2,1-b]thiazole; Formate | 374.492 |  | * |
| KP | 2-[3-(5-Bromo-2-methoxy-phenylsulfanyl)-propyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 389.3177 |  | * |
| KQ | 2-[2-(2-Methoxy-5-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | 380.4339 |  | *** |
| KR | 9-Methyl-10-naphthalen-1-yl-2,3,9,10-tetrahydro-1H-4,9,10a-triazaphenanthrene; Formate | 373.459 |  | * |
| KS | 7-Chloro-4,8-dimethyl-1H-quinolin-2-one | 207.6592 |  | * |
| KT | 7-Chloro-4-methyl-2-piperazin-1-yl-quinoline | 261.754 |  | * |
| KU | 4,8-Dimethyl-2-piperazin-1-yl-quinoline | 241.3361 |  | * |
| KV | 2-[4-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 374.9574 |  | ** |
| KW | 2-[2-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 374.9574 |  | *** |
| KX | 6-(2-Methoxy-phenyl)-3,4-dihydro-2H-pyrimido[2,1-a]isoquinoline; Formate | 336.3948 |  | * |

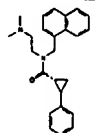
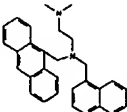
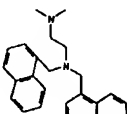
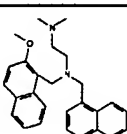
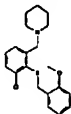
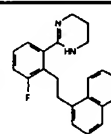
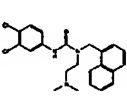
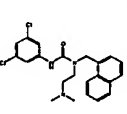
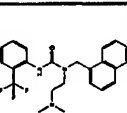
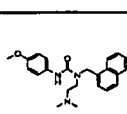
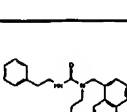
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|----|--|----------|---|-----|
| KY | Piperazine | 86.1369 |  | * |
| KZ | 2-[2-(4-Fluoro-naphthalen-1-ylmethylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HBr | 431.3717 |  | *** |
| LA | 7-Ethyl-4-methyl-2-piperazin-1-yl-quinoline | 255.363 |  | * |
| LB | 8-Ethyl-4-methyl-2-piperazin-1-yl-quinoline | 255.363 |  | * |
| LC | 5,8-Dimethoxy-4-methyl-2-piperazin-1-yl-quinoline | 287.3618 |  | * |
| LD | 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Parent | 441.2909 |  | *** |
| LE | 2-[2-(2-Naphthalen-1-yl-ethyl)-3-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine; HCl | 418.8884 |  | *** |
| LF | 2-[4-Benzoyloxy-2-(5-bromo-2-methoxy-benzylsulfonyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine; Formate | 543.4858 |  | ** |
| LG | [3-(5-Bromo-2-methoxy-benzylsulfonyl)-quinoxalin-2-yl]-[3-pyrrolidin-1-yl-propyl]-amine; formate | 533.4937 |  | * |
| LH | Naphthalen-1-ylmethyl-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine; Formate | 361.448 |  | * |
| LI | [3-(5-Bromo-2-methoxy-benzylsulfonyl)-quinoxalin-2-yl]-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-amine; Formate | 533.4937 |  | * |

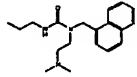
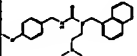
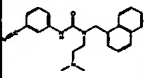
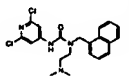
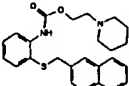
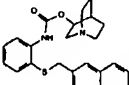
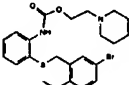
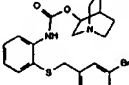
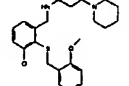
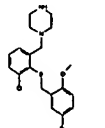
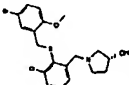
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|----|--|----------|---|-----|
| LJ | [3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-[3-(2-methyl-piperidin-1-yl)-propyl]-amine; Formate | 561.5475 |  | * |
| LK | [3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-piperidin-4-ylmethyl-amine; Formate | 519.4669 |  | * |
| LM | 2-[1,4]Bipiperidinyl-1'-yl-3-(5-bromo-2-methoxy-benzylsulfanyl)-quinoxaline; Formate | 573.5585 |  | * |
| LN | N1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-propane-1,3-diamine; 2HCl | 506.2935 |  | * |
| LO | 2-[1,4]Bipiperidinyl-1'-yl-3-(5-bromo-2-methoxy-benzylsulfanyl)-quinoxaline; Formate | 581.5377 |  | * |
| LP | 2-[5-Bromo-2-methoxy-benzylsulfanyl]-3-[4-(3-morpholin-4-yl-propyl)-piperazin-1-yl]-quinoxaline; Formate | 618.5995 |  | * |
| LQ | 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-piperidine-1-carboxylic acid ethyl ester; Formate | 539.4949 |  | * |
| LR | 1-[2-(Naphthalen-1-ylmethylsulfanyl)-benzyl]-piperidine | 347.5242 |  | * |
| LS | 2-[4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperazin-1-yl]-pyrimidine; Formate | 531.4779 |  | * |
| LT | 2-[2-(6-Fluoro-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidino; HBr | 431.3717 |  | ... |
| LU | 1-[4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperazin-1-yl]-ethanone; Formate | 495.4418 |  | * |

| | | | | |
|----|---|----------|---|-----|
| LV | 2-[2-[4-[2-(5-Bromo-2-methoxybenzylsulfonyl)-benzyl]-piperazin-1-yl]-ethoxy]-ethanol; Formate | 541.5108 |  | * |
| LW | 2-[4-[2-(5-Bromo-2-methoxybenzylsulfonyl)-benzyl]-piperazin-1-yl]-N-isopropylacetamide; Formate | 552.5371 |  | ** |
| LX | [1-[2-(5-Bromo-2-methoxybenzylsulfonyl)-benzyl]-piperidin-2-yl]-methanol; Formate | 482.443 |  | *** |
| LY | 1-[2-(5-Bromo-2-methoxybenzylsulfonyl)-benzyl]-2-(N-pyrrolo)methylpyrrolidine; Formate | 521.523 |  | * |
| LZ | 1'-[2-(5-Bromo-2-methoxybenzylsulfonyl)-benzyl]-[1,4']piperidiny; Formate | 535.5499 |  | * |
| MA | 1-[2-(5-Bromo-2-methoxybenzylsulfonyl)-benzyl]-4-cycloheptyl-piperazine; Formate | 549.5768 |  | * |
| MB | 3-[2-[2-(1,4,5,6-Tetrahydropyrimidin-2-yl)-phenyl]-ethyl]-1H-indole | 349.437 |  | * |
| MC | N'-[3-(5-Bromo-2-methoxybenzylsulfonyl)-quinoxalin-2-yl]-N,N-diethyl-ethane-1,2-diamine; Formate | 521.4827 |  | * |
| MD | N'-[3-(5-Bromo-2-methoxybenzylsulfonyl)-quinoxalin-2-yl]-N,N-dimethylpropane-1,3-diamine; Formate | 507.4559 |  | * |
| ME | 2-(5-Bromo-2-methoxybenzylsulfonyl)-3-[1,4]diazepan-1-yl quinoxaline; Formate | 505.44 |  | * |
| MF | N-(4-Bromo-benzyl)-N',N'-dimethyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine | 397.358 |  | * |

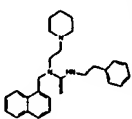
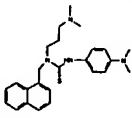
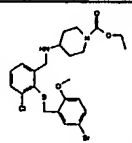
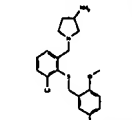
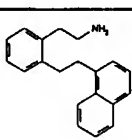
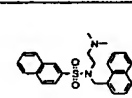
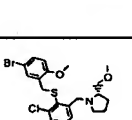

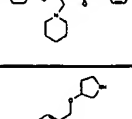
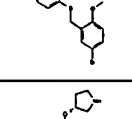
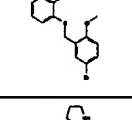
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|----|--|----------|---|----|
| MG | 3'-[5-Bromo-2-methoxy-benzylsulfanyl]-4-(3-morpholin-4-yl-propyl)-3,4,5,6-tetrahydro-2H-[1,2]bipyrazinyl Formate | 568.5396 |  | * |
| MH | [3-[3'-(5-Bromo-2-methoxy-benzylsulfanyl)-2,3,5,6-tetrahydro[1,2]bipyrazinyl-4-yl]-propyl]-dimethyl-amine; Formate | 526.5023 |  | * |
| MI | N-(3-Bromo-benzyl)-N-(5-bromo-2-methoxy-benzyl)-N',N'-dimethyl-ethane-1,2-diamine | 456.2204 |  | * |
| MJ | N-(1-Benzyl-piperidin-4-yl)-2-(naphthalen-1-ylmethylsulfanyl)-benzamide | 466.6471 |  | * |
| MK | N,N-Dimethyl-N'-naphthalen-2-ylmethyl-N'-naphthalen-1-ylmethyl-ethane-1,2-diamine | 368.5218 |  | * |
| ML | 8-Methyl-3-[2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-8-azabicyclo[3.2.1]octa-n-3-ol; Formate | 435.5915 |  | ** |
| MM | 1-Methyl-4-[2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-piperidin-4-ol; Formate | 409.5536 |  | * |
| MN | 3-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-1-azabicyclo[2.2.2]octa-n-3-ol; Formate | 421.5646 |  | * |
| MO | 1'-[3-[5-Bromo-2-methoxy-benzylsulfanyl]-pyrazin-2-yl]-[1,4]bipiperidinyl | 477.4686 |  | * |
| MP | [3-[5-Bromo-2-methoxy-benzylsulfanyl]-pyrazin-2-yl]-[2-(1-methyl-pyrrolidin-2-yl)-ethyl]-amine | 437.4039 |  | * |
| MQ | [3-[5-Bromo-2-methoxy-benzylsulfanyl]-pyrazin-2-yl]-[3-(2-methyl-piperidin-1-yl)-propyl]-amine | 465.4576 |  | * |

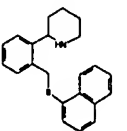
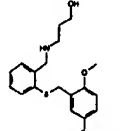
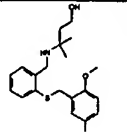
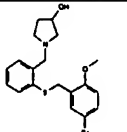
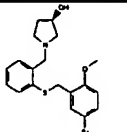
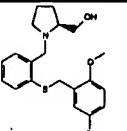
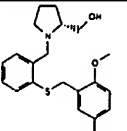
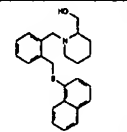
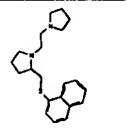
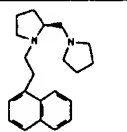
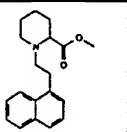
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|----|---|----------|---|----|
| MR | N-(3-Chloro-benzyl)-N-(2-methoxy-benzyl)-N,N'-dimethyl-ethane-1,2-diamine | 332.8731 |  | * |
| MS | N-(3-Bromo-benzyl)-N,N'-dimethyl-N-(4-methyl-benzyl)-ethane-1,2-diamine | 381.7429 |  | * |
| MT | N-(3-Bromo-benzyl)-N,N'-dimethyl-N-naphthalen-2-ylmethyl-ethane-1,2-diamine | 397.358 |  | * |
| MU | N-(3-Bromo-benzyl)-N,N'-dimethyl-N-(4-methyl-benzyl)-ethane-1,2-diamine | 361.325 |  | * |
| MV | N-Benzyl-N-(2-methoxy-benzyl)-N,N'-dimethyl-ethane-1,2-diamine | 298.4283 |  | * |
| MW | N-Benzyl-N-(2-chloro-benzyl)-N,N'-dimethyl-ethane-1,2-diamine | 302.8468 |  | * |
| MX | N-Benzyl-N,N'-dimethyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine | 318.4619 |  | * |
| MY | N-(5-Bromo-2-methoxy-benzyl)-N,N'-dimethyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine | 427.3843 |  | * |
| MZ | 8-Methyl-3-[2-(naphthalen-1-ylsulfonylmethyl)-phenyl]-8-aza-bicyclo[3.2.1]oct-2-ene | 371.5462 |  | ** |
| NA | 1-Ethyl-3-[2-(naphthalen-1-ylsulfonylmethyl)-phenyl]-piperidin-3-ol; Formate | 423.5805 |  | * |
| NB | 1-Methyl-4-[2-(naphthalen-1-ylsulfonylmethyl)-phenyl]-1,2,3,6-tetrahydropyridine; Formate | 391.5384 |  | ** |

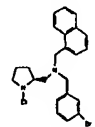
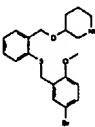
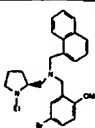
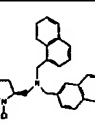
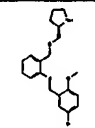
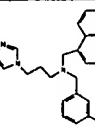
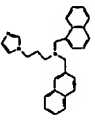
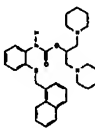
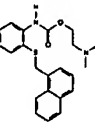
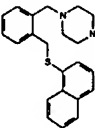
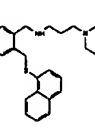
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|----|---|----------|---|-----|
| NC | 2-Phenyl-cyclopropanecarboxylic acid (2-dimethylaminoethyl)-naphthalen-1-ylmethyl-amide | 372.5102 |  | * |
| ND | N-Anthracen-9-ylmethyl-N,N'-dimethyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine | 418.5817 |  | * |
| NE | N,N-Dimethyl-N,N'-bis-naphthalen-1-ylmethyl-ethane-1,2-diamine | 368.5218 |  | * |
| NF | N-(2-Methoxynaphthalen-1-ylmethyl)-N,N'-dimethyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine | 398.5481 |  | * |
| NG | 1-{2-(5-Bromo-2-methoxybenzylsulfanyl)-3-chloro-benzyl}-piperidine | 440.8315 |  | * |
| NH | 2-{3-Fluoro-2-(2-naphthalen-1-ylethyl)-phenyl}-1,4,5,6-tetrahydropyrimidine; HCl | 368.8806 |  | *** |
| NI | 3-(3,4-Dichlorophenyl)-1-(2-dimethylaminoethyl)-1-naphthalen-1-ylmethyl-urea | 416.3496 |  | * |
| NJ | 3-(3,5-Dichlorophenyl)-1-(2-dimethylaminoethyl)-1-naphthalen-1-ylmethyl-urea | 416.3496 |  | * |
| NK | 1-(2-Dimethylaminoethyl)-1-naphthalen-1-ylmethyl-3-(2-trifluoromethylphenyl)-urea | 415.4584 |  | * |
| NL | 1-(2-Dimethylaminoethyl)-3-(4-methoxy-phenyl)-1-naphthalen-1-ylmethyl-urea | 377.4864 |  | * |
| NM | 1-(2-Dimethylaminoethyl)-1-naphthalen-1-ylmethyl-3-phenylethyl-urea | 375.5139 |  | * |

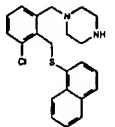
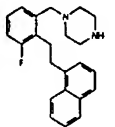
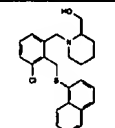
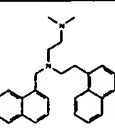
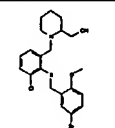
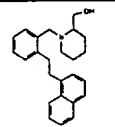
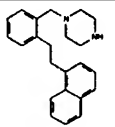
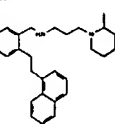
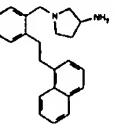
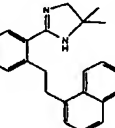
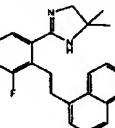
| | | | | |
|----|---|----------|---|-----|
| NN | 1-(2-Dimethylaminoethyl)-1-naphthalen-1-ylmethyl-urea | 313.443 |  | * |
| NO | 1-(2-Dimethylaminoethyl)-3-(4-methoxy-benzyl)-1-naphthalen-1-ylmethyl-urea | 391.5133 |  | * |
| NP | 3-(3-Cyano-phenyl)-1-(2-dimethylaminoethyl)-1-naphthalen-1-ylmethyl-urea | 372.4699 |  | * |
| NQ | 3-(2,6-Dichloro-pyridin-4-yl)-1-(2-dimethylaminoethyl)-1-naphthalen-1-ylmethyl-urea | 417.3374 |  | * |
| NR | [2-(Naphthalen-2-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester; formate | 466.6056 |  | * |
| NS | [2-(Naphthalen-2-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester; formate | 464.5897 |  | * |
| NT | [2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester | 525.4681 |  | ** |
| NU | [2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester; formate | 523.4522 |  | * |
| NV | [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-3-(2-methyl-piperidin-1-yl)-propyl]-amine; 2HCl | 584.8751 |  | *** |
| NW | 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperazine; 2HCl | 514.7407 |  | *** |
| NX | 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pymolidin-3-ol; Formate | 488.834 |  | * |

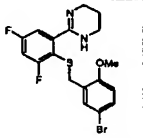
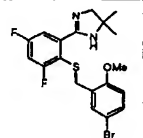
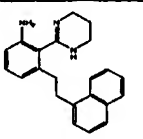
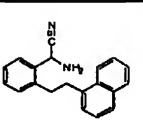
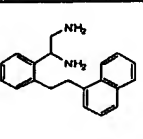
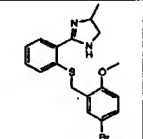
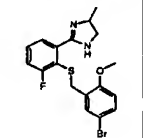
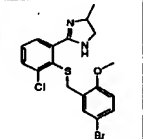
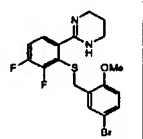
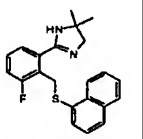
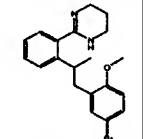
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|----|--|----------|--|----|
| NY | 1-{2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl}-pyrrolidin-2-yl-methanol; Formate | 502.8609 | | * |
| NZ | 1-{2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl}-azetidine; Formate | 458.8077 | | * |
| OA | 1-{2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl}-pyrrolidin-3-ol; Formate | 488.834 | | * |
| OB | [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester; Formate | 464.5897 | | * |
| OC | [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester; Formate | 478.6166 | | ** |
| OD | [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester; Formate | 480.6325 | | * |
| OE | 1-{2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl}-pyrrolidin-2-yl-methanol; Formate | 502.8609 | | * |
| OF | Naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-(2-piperidin-1-yl-ethyl)-amine | 408.5866 | | * |
| OG | 4-tert-Butyl-N-naphthalen-1-ylmethyl-N-(2-piperidin-1-yl-ethyl)-benzamide | 428.6177 | | * |
| OH | N,N-Dimethyl-N'-naphthalen-2-ylmethyl-N'-naphthalen-1-ylmethyl-propane-1,3-diamine | 382.5487 | | * |
| OI | N-(5-Bromo-2-methoxy-benzyl)-N',N'-dimethyl-N-naphthalen-1-ylmethyl-propane-1,3-diamine | 441.4111 | | * |

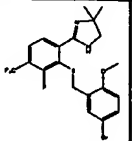
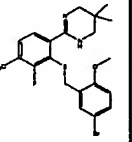
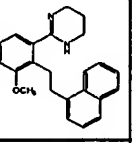
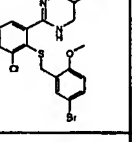
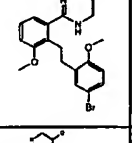
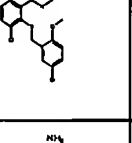
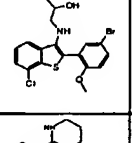
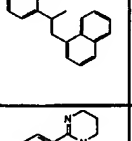
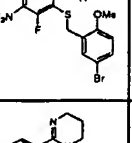
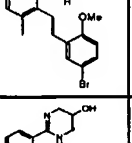
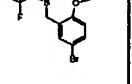
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|----|---|----------|---|-----|
| OJ | 1-Naphthalen-1-ylmethyl-3-phenethyl-1-(2-piperidin-1-ylethyl)-thiourea; HCl | 468.1052 |  | * |
| OK | 3-(4-Dimethylamino-phenyl)-1-(3-dimethylamino-propyl)-1-naphthalen-1-ylmethyl-thiourea; HCl | 457.082 |  | *** |
| OL | 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzylamino]-piperidine-1-carboxylic acid ethyl ester; Formate | 573.9397 |  | ** |
| OM | 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ylamine; 2HCl | 514.7407 |  | *** |
| ON | 2-[2-(2-Naphthalen-1-ylethyl)-phenyl]-ethylamine; HCl | 311.8535 |  | ** |
| OO | Naphthalene-2-sulfonic acid (2-dimethylamino-ethyl)-naphthalen-1-ylmethyl-amide | 418.5597 |  | * |
| OP | 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-2-methoxymethyl-pyrrolidine; Formate | 516.8877 |  | * |
| OQ | (2-Hexyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester; Formate | 491.6758 |  | ** |
| OR | 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-pyrrolidine; HCl | 444.8192 |  | ** |
| OS | 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-pyrrolidine; HCl | 444.8192 |  | ** |
| OT | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine; HCl | 458.8461 |  | ** |

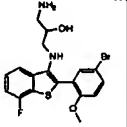
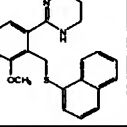
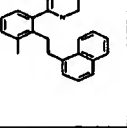
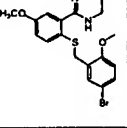
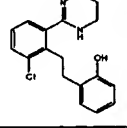
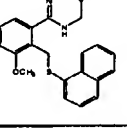
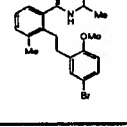
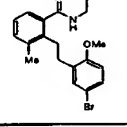
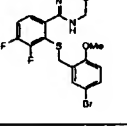
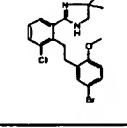
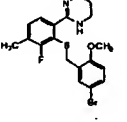
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|----|--|----------|---|----|
| OU | 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-piperidine; HCl | 369.9574 |  | * |
| OV | 3-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzylamino]-propan-1-ol | 396.3482 |  | * |
| OW | 3-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzylamino]-3-methyl-butan-1-ol | 424.402 |  | ** |
| OX | 1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzyl]-pyrrolidin-3-ol | 408.3592 |  | * |
| OY | 1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzyl]-pyrrolidin-3-ol | 408.3592 |  | * |
| OZ | [1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzyl]-pyrrolidin-2-yl]-methanol | 422.3861 |  | * |
| PA | [1-[2-(5-Bromo-2-methoxybenzylsulfanyl)-benzyl]-pyrrolidin-2-yl]-methanol | 422.3861 |  | * |
| PB | [1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl]-methanol; Formate | 423.5805 |  | * |
| PC | 2-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-ethyl-N-pyrrolidine; Formate | 386.5628 |  | * |
| PD | N-pyrrolyl-[1-[2-naphthalen-1-yl-ethyl]-pyrrolidin-2-ylmethyl]-amine | 308.4668 |  | * |
| PE | 1-[2-(Naphthalen-1-yl-ethyl)-piperidine-2-carboxylic acid methyl ester | 297.3972 |  | * |

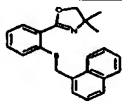
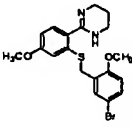
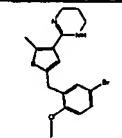
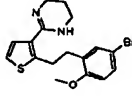
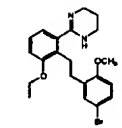
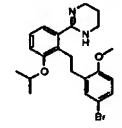
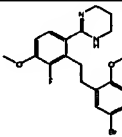
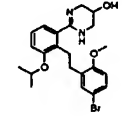
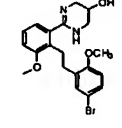
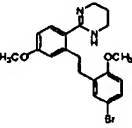
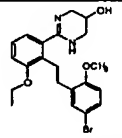
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|----|---|----------|---|----|
| PF | (3-Bromo-benzyl) (1-ethyl-pyrrolidin-2-ylmethyl)- naphthalen-1-ylmethyl-amine | 437.4227 |  | * |
| PG | 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzoyloxy]- piperidine; HCl | 458.8461 |  | ** |
| PH | (5-Bromo-2-methoxy-benzyl)- (1-ethyl-pyrrolidin-2-ylmethyl)- naphthalen-1-ylmethyl-amine | 467.449 |  | * |
| PI | (1-Ethyl-pyrrolidin-2-ylmethyl)- naphthalen-2-ylmethyl- naphthalen-1-ylmethyl-amine | 408.5866 |  | * |
| PJ | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzoyloxymethyl]- pyrrolidine; HCl | 458.8461 |  | ** |
| PK | (3-Bromo-benzyl) (3-imidazol-1-yl-propyl)- naphthalen-1-ylmethyl-amine | 434.3788 |  | * |
| PL | (3-imidazol-1-yl-propyl)- naphthalen-2-ylmethyl- naphthalen-1-ylmethyl-amine | 405.5426 |  | * |
| PM | [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester; Formate | 563.7657 |  | * |
| PN | [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-dimethylamino-ethyl ester; Formate | 426.5408 |  | * |
| PO | 1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]- piperazine; Formate | 394.542 |  | ** |
| PP | [3-(2-Methyl-piperidin-1-yl-propyl)]-2-(naphthalen-1-ylsulfanylmethyl)- benzyl]-amine; Formate | 464.6764 |  | ** |

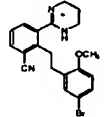
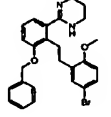
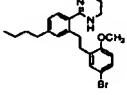
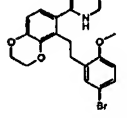
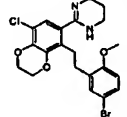
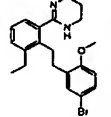
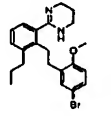
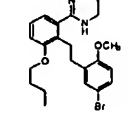
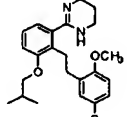
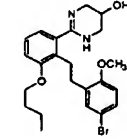
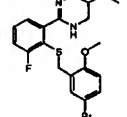
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|----|---|----------|---|-----|
| PQ | 1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine; HCl | 419.4168 |  | .. |
| PR | 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine; HCl | 384.9234 |  | ... |
| PS | {1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol; Formate | 458.0253 |  | * |
| PT | N,N-Dimethyl-N'-(2-naphthalen-1-yl-ethyl)-N'-naphthalen-1-ylmethoxy-ethane-1,2-diamine; Formate | 428.5787 |  | * |
| PU | {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol | 470.8577 |  | * |
| PV | {1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperidin-2-yl}-methanol; Formate | 405.5414 |  | * |
| PW | 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperazine; Formate | 376.5029 |  | * |
| PX | [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine; Formate | 446.6373 |  | * |
| PY | 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-pyrrolidin-3-ylamine; Formate | 376.5029 |  | .. |
| PZ | 5,5-Dimethyl-2-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole | |  | ... |
| QA | 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole | |  | ... |

| | | | |
|----|---|---|-----|
| QB | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluorophenyl]-1,4,5,6-tetrahydro-pyrimidine |  | *** |
| QC | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluorophenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole |  | ** |
| QD | 3-[2-Naphthalen-1-yl-ethyl]-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine |  | * |
| QE | Amino-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-acetonitrile |  | * |
| QF | 1-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethane-1,2-diamine |  | ** |
| QG | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4-methyl-4,5-dihydro-1H-imidazole |  | ** |
| QH | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole |  | *** |
| QI | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole |  | *** |
| QJ | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluorophenyl]-1,4,5,6-tetrahydro-pyrimidine |  | *** |
| QK | 2-[3-Fluoro-2-(naphthalen-1-yl)sulfanylmethyl]-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole |  | ** |
| QL | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-1-methylethyl]-phenyl]-1,4,5,8-tetrahydro-pyrimidine |  | *** |

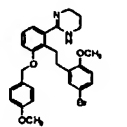
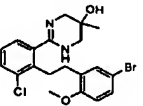
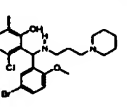
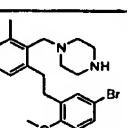
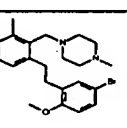
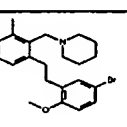
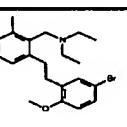
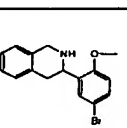
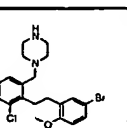
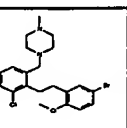
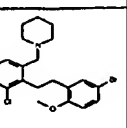
| | | | |
|----|--|---|-----|
| QM | 2-[2-(5-Bromo-2-methoxy-benzyl-sulfonyl)-3-fluoro-4-trifluoromethyl-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole |  | * |
| QN | 2-[2-(5-Bromo-2-methoxy-benzyl-sulfonyl)-3-fluoro-4-trifluoromethyl-phenyl]-8,8-dimethyl-1,4,5,6-tetrahydro-pyrimidine |  | * |
| QO | 2-[3-Methoxy-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine |  | *** |
| QP | 2-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol |  | *** |
| QQ | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine |  | *** |
| QR | 2-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol |  | *** |
| QS | 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-chloro-benzotriophen-3-ylamino]-propan-2-ol |  | * |
| QT | 2-[2-(1-Methyl-2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine |  | ** |
| QU | 3-(5-Bromo-2-methoxy-benzylsulfonyl)-2-fluoro-4-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine |  | * |
| QV | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine |  | *** |
| QW | 2-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol |  | *** |

| | | | |
|----|--|---|-----|
| QX | 1-Amino-3-[2-(5-bromo-2-methoxyphenyl)-7-fluorobenzo[b]thiophen-3-ylamino]-propan-2-ol |  | * |
| QY | 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine |  | *** |
| QZ | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol |  | *** |
| RA | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine |  | ** |
| RB | 2-[2-[2-Chloro-6-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-ethyl]-phenol |  | *** |
| RC | 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol |  | *** |
| RD | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl]-5-methyl-4,5-dihydro-1H-imidazole |  | *** |
| RE | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol |  | *** |
| RF | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol |  | ** |
| RG | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole |  | *** |
| RH | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-4-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine |  | ** |

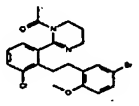
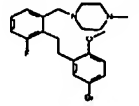
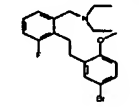
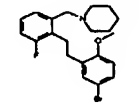
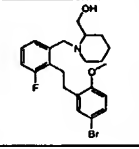
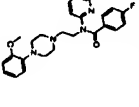
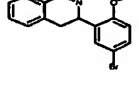
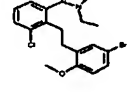
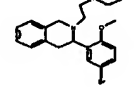
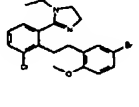
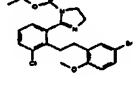
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|----|--|---|-----|
| RI | 4,4-Dimethyl-2-[2-(naphthalen-1-ylmethanesulfonyl)-phenyl]-4,5-dihydro-oxazole |  | * |
| RJ | 2-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-4-methoxy-phenyl]-1,4,5,6-tetrahydro pyrimidine |  | * |
| RK | 2-[5-(5-Bromo-2-methoxy-benzyl)-2-methyl-thiophen-3-yl]-1,4,5,6-tetrahydro pyrimidine |  | ** |
| RL | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl]-1,4,5,6-tetrahydro pyrimidine |  | *** |
| RM | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl]-1,4,5,6-tetrahydro pyrimidine |  | *** |
| RN | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl]-1,4,5,6-tetrahydro pyrimidine |  | *** |
| RO | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-4-methoxy-phenyl]-1,4,5,6-tetrahydro pyrimidine |  | * |
| RP | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl]-1,4,5,6-tetrahydro pyrimidin-5-ol |  | ** |
| RQ | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl]-1,4,5,6-tetrahydro pyrimidin-5-ol |  | *** |
| RS | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-methoxy-phenyl]-1,4,5,6-tetrahydro pyrimidine |  | * |
| RT | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl]-1,4,5,6-tetrahydro pyrimidin-5-ol |  | *** |

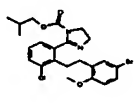
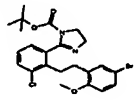
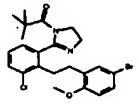
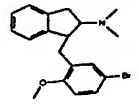
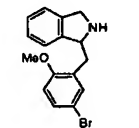
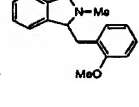
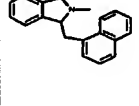
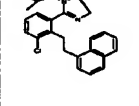
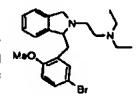
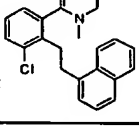
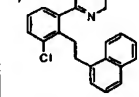
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|----|--|--|---|-----|
| RU | 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(1,4,5,8-tetrahydro-pyrimidin-2-yl)-benzonitrile | |  | *** |
| RV | 2-[3-Benzoyloxy-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-phenyl]-1,4,5,8-tetrahydro-pyrimidine | |  | * |
| RW | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-butyl-phenyl]-1,4,5,8-tetrahydro-pyrimidine | |  | * |
| RX | 2-[5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-2,3-dihydro-benzof[1,4]dioxin-6-yl]-1,4,5,8-tetrahydro-pyrimidine | |  | ** |
| RY | 2-[5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-8-chloro-2,3-dihydro-benzof[1,4]dioxin-6-yl]-1,4,5,8-tetrahydro-pyrimidine | |  | ** |
| RZ | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethyl-phenyl]-1,4,5,8-tetrahydro-pyrimidine | |  | *** |
| SA | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propyl-phenyl]-1,4,5,8-tetrahydro-pyrimidine | |  | *** |
| SB | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl]-1,4,5,8-tetrahydro-pyrimidine | |  | ** |
| SC | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isobutoxy-phenyl]-1,4,5,8-tetrahydro-pyrimidine | |  | ** |
| SD | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl]-1,4,5,8-tetrahydro-pyrimidin-5-ol | |  | ** |
| SE | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5-methoxy-1,4,5,8-tetrahydro-pyrimidine | |  | *** |

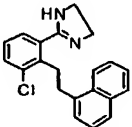
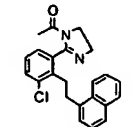
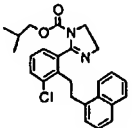
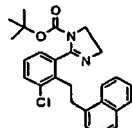
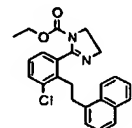
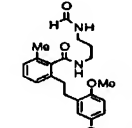
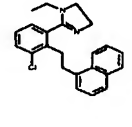
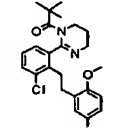
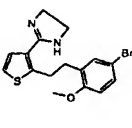
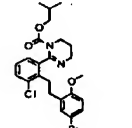
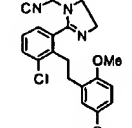
| | | | |
|----|--|--|-----|
| SF | 2-[2-(2-(5-Bromo-2-methoxy-phenyl)-ethyl)-3-chloro-phenyl]-1-methyl-1,4,5,6-tetrahydro-pyrimidine | | ... |
| SG | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole | | ... |
| SH | [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole | | ... |
| SI | 2-[2-[3-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-biphenyl-2-yl]-ethyl]-phenol | | ... |
| SJ | 2-[2-(2-(5-Bromo-2-methoxy-phenyl)-ethyl)-3-chloro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole | | ... |
| SK | N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methoxy-benzamide | | * |
| SL | N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzamide | | * |
| SM | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-2-methyl-propyl ester | | ... |
| SN | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester | | ** |
| SO | 2-[3-Methoxy-2-[2-(2-methoxy-phenyl)-ethyl]-phenyl]-1,4,5,6-tetrahydro-pyrimidine | | ** |
| SP | 3-(5-Bromo-2-methoxy-phenyl)-5-chloro-3,4-dihydro-isoquinolin-1-ylamine | | ** |

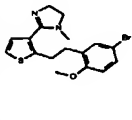
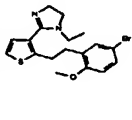
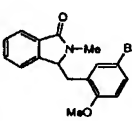
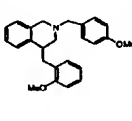
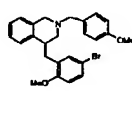
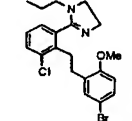
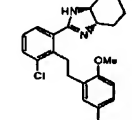
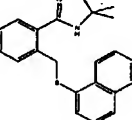
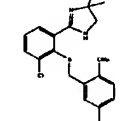
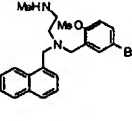
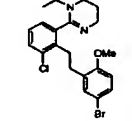
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|----|--|--|---|-----|
| SQ | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(4-methoxy-benzoyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine | |  | ** |
| SR | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-5-methyl-1,4,5,6-tetrahydro-pyrimidin-5-ol | |  | *** |
| SS | 2-[5-Bromo-2-methoxy-phenyl]-3-piperidin-1-yl-propylamino-methyl-3-chloro-6-methyl-phenol | |  | ** |
| ST | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl]-piperazine | |  | *** |
| SU | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl]-4-methyl-piperazine | |  | ** |
| SV | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl]-piperidine | |  | * |
| SW | [2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl]-diethyl-amine | |  | ** |
| SY | 3-(5-Bromo-2-methoxy-phenyl)-1,2,3,4-tetrahydro-isoquinoline | |  | * |
| SX | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl]-piperazine | |  | ** |
| SY | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl]-4-methyl-piperazine | |  | * |
| SZ | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl]-piperidine | |  | * |

| | | | |
|----|---|--|-----|
| TA | 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl-diethyl-amine | | ** |
| TB | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-4,5-dihydro-1H-imidazole | | *** |
| TC | (1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl]-piperidin-2-yl)-methanol | | ** |
| TD | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl]-1,4,5,6-tetrahydro pyrimidine | | *** |
| TE | 1-[2-(5-Bromo-2-methoxy-benzyl)sulfonyl]-benzyl-4-methyl-piperazine | | * |
| TF | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl]-piperazine | | ** |
| TG | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl]-4-methyl-piperazine | | * |
| TH | 1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl]-piperidine | | * |
| TI | 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl-diethyl-amine | | * |
| TJ | 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isindole | | * |
| TK | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-5,6-dihydro-4H-pyrimidine 1-carboxylic acid 1-acetoxyl-ethyl ester | | *** |

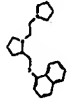
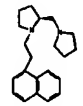
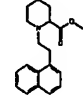
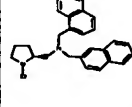
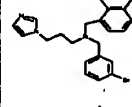
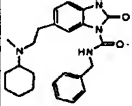
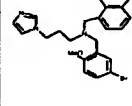
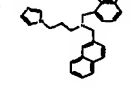
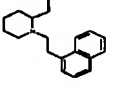
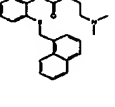
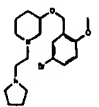
| | | | | |
|----|--|--|---|-----|
| TL | 1-(2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl)-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone | |  | ... |
| TM | 1-(2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl)-4-methyl-piperazine | |  | ... |
| TN | (2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl)-diethyl-amine | |  | ... |
| TO | 1-(2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl)-piperidine | |  | .. |
| TP | (1-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl]-piperidin-2-yl)-methanol | |  | .. |
| TQ | 4-Fluoro-N-[2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl]-N-pyridin-2-yl-benzamide | |  | . |
| TR | 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline | |  | . |
| TS | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-1-ethyl-4,5-dihydro-1H-imidazole | |  | ... |
| TT | [2-[3-(5-Bromo-2-methoxy-phenyl)-3,4-dihydro-1H-isoquinolin-2-yl]-ethyl]-diethyl-amine | |  | . |
| TU | 1-(2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-4,5-dihydro-imidazol-1-yl)-ethanone | |  | . |
| TV | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester | |  | . |

| | | | |
|----|--|---|-----|
| TW | 2-[2-{2-(5-Bromo-2-methoxy-phenyl)-ethyl-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester |  | * |
| TX | 2-[2-{2-(5-Bromo-2-methoxy-phenyl)-ethyl-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester |  | * |
| TY | 1-[2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl-3-chloro-phenyl]-4,5-dihydro-imidazol-1-yl}-2,2-dimethyl-propan-1-one |  | ** |
| TZ | [1-(5-Bromo-2-methoxy-benzyl)-indan-2-yl]-dimethyl-amine |  | * |
| UA | 1-(5-Bromo-2-methoxy-benzyl)-2,3-dihydro-1H-isindole |  | * |
| UB | 1-(2-Methoxy-benzyl)-2-methyl-2,3-dihydro-1H-isindole |  | * |
| UC | 2-Methyl-1-naphthalen-1-ylmethyl-2,3-dihydro-1H-isindole |  | * |
| UD | 1-[2-{3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl}-4,5-dihydro-imidazol-1-yl]-2,2-dimethyl-propan-1-one |  | * |
| UE | [2-{1-(5-Bromo-2-methoxy-benzyl)-1,3-dihydro-isindol-2-yl}-ethyl]-diethyl-amine |  | ** |
| UF | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-1,4,5,6-tetrahydro-pyrimidine |  | *** |
| UG | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid tert-butyl ester |  | *** |

| | | | |
|----|---|---|-----|
| UH | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole |  | ... |
| UI | 1-[2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl]-ethanone |  | * |
| UJ | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester |  | * |
| UK | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester |  | * |
| UL | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester |  | * |
| UM | 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-N-(3-formylamino-propyl)-6-methylbenzamide |  | * |
| UN | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-ethyl-4,5-dihydro-1H-imidazole |  | ... |
| UO | 1-[2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-5,6-dihydro-4H-pyrimidin-yl]-2,2-dimethylpropan-1-one |  | * |
| UP | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl]-4,5-dihydro-1H-imidazole |  | ... |
| UQ | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid isobutyl ester |  | * |
| UR | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-1-isocyanomethyl-4,5-dihydro-1H-imidazole |  | ... |

| | | | |
|----|---|---|-----|
| US | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl]-1-methyl-4,5-dihydro-1H-imidazole |  | *** |
| UT | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl]-1-ethyl-4,5-dihydro-1H-imidazole |  | *** |
| UU | 3-(5-Bromo-2-methoxy-benzyl)-2-methyl-2,3-dihydro-isindol-1-one |  | * |
| UX | 4-(2-Methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydroisoquinoline |  | * |
| UW | 4-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydroisoquinoline |  | * |
| UY | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-1-propyl-4,5-dihydro-1H-imidazole |  | *** |
| UZ | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzimidazole |  | *** |
| VA | 5,5-Dimethyl-2-[2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole |  | *** |
| VB | 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole |  | *** |
| VC | N-(5-Bromo-2-methoxy-benzyl)-N'-methyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine |  | ** |
| VD | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-1-ethyl-1,4,5,6-tetrahydropyrimidine |  | *** |

| | | | |
|----|--|--|-----|
| VE | 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-N,N,N'-trimethyl-benzamidino | | *** |
| VF | 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-4,5-dihydro-1H-imidazole | | *** |
| VG | 1-Benzyl-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-4,5-dihydro-1H-imidazole | | *** |
| VH | [(2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl)-pyrrolidin-1-yl]-methyl-amine | | ** |
| VI | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-1-isopropyl-4,5-dihydro-1H-imidazole | | *** |
| VJ | 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl]-1-(2,2,2-trifluoroethyl)-4,5-dihydro-1H-imidazole | | *** |
| VK | 1-[2-(2-(5-Bromo-2-methoxy-benzylsulfonyl)-benzyloxy)-ethyl]-aziridine | | * |
| VL | 3-[2-(5-Bromo-2-methoxy-benzylsulfonyl)-benzylamino]-3-methyl-butan-1-ol | | * |
| VM | 3-Cyano-N-(2-dimethylamino-ethyl)-N-naphthalen-1-ylmethylbenzamide | | * |
| VN | N-(2-Dimethylamino-ethyl)-4-fluoro-N-naphthalen-1-ylmethylbenzenesulfonamide | | * |
| VO | 2-Cyano-N-(2-dimethylamino-ethyl)-N-naphthalen-1-ylmethylbenzenesulfonamide | | * |

| | | | |
|----|--|---|---|
| VP | 2-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-ethyl-1-pyrrolidine |  | . |
| VQ | C-[1-(2-Naphthalen-1-yl-ethyl)-pyrrolidin-2-yl]-methyl-1-pyrrolidine |  | . |
| VR | 1-(2-Naphthalen-1-yl-ethyl)-piperidine-2-carboxylic acid methyl ester |  | . |
| VS | (1-Ethyl-pyrrolidin-2-ylmethyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine |  | . |
| VT | (3-Bromo-benzyl)-(3-imidazol-1-yl-propyl)-naphthalen-1-ylmethyl-amine |  | . |
| VU | 6-[2-(Cyclohexylmethyl-amine)-ethyl]-2-oxo-2,3-dihydro-benzimidazole-1-carboxylic acid benzylamide |  | . |
| VV | (5-Bromo-2-methoxy-benzyl)-(3-imidazol-1-yl-propyl)-naphthalen-1-ylmethyl-amine |  | . |
| VW | (3-imidazol-1-yl-propyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine |  | . |
| VX | Dimethyl-[1-(2-naphthalen-1-yl-ethyl)-piperidin-2-ylmethyl]-amine |  | . |
| VY | [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-dimethylamino-ethyl ester |  | . |
| VZ | 3-(5-Bromo-2-methoxy-benzyl)-1-[2-pyrrolidin-1-yl-ethyl]-piperidine |  | . |





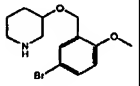
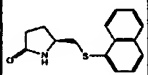



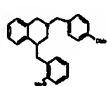
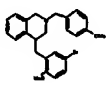
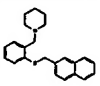
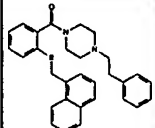
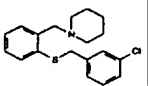
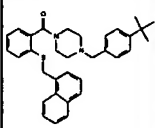
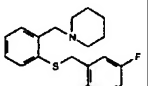
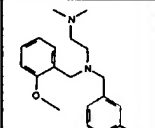
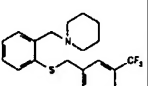
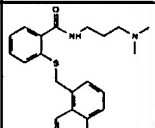
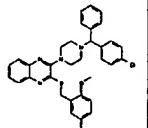
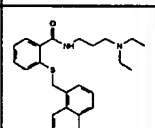
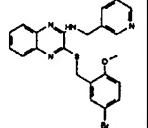
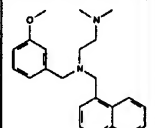
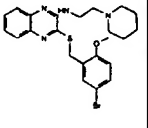
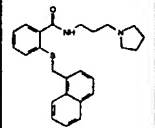
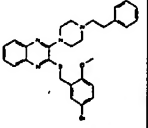
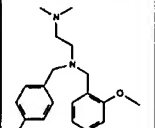
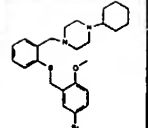
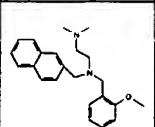
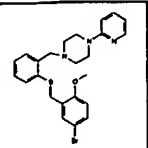
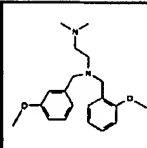
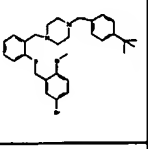
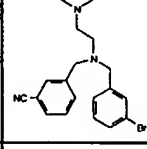
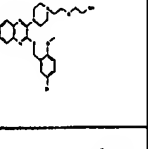
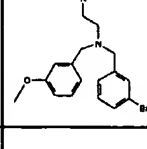
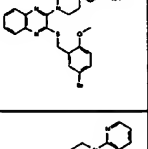
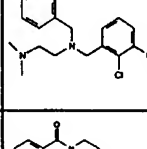
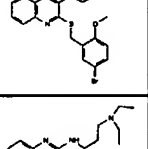
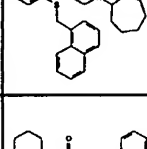
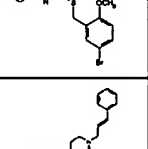
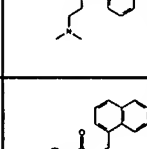
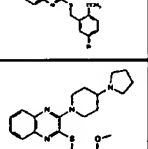
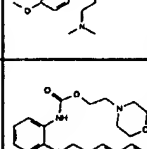
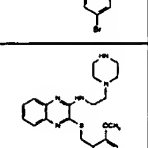
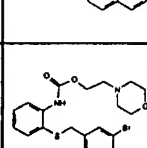
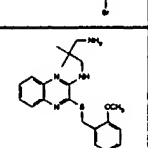
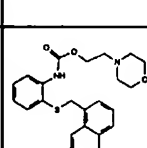
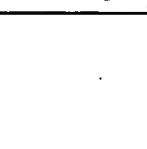
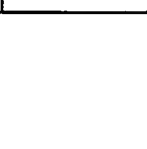
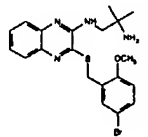
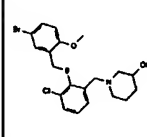
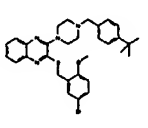
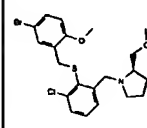
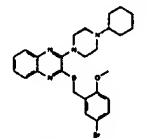
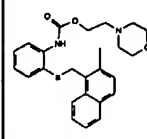
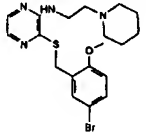
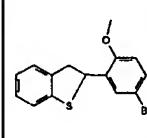
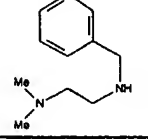
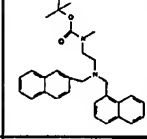
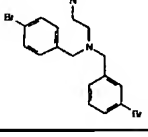
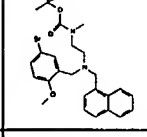
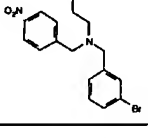
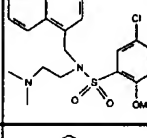
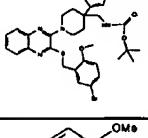
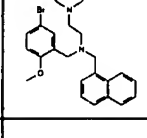
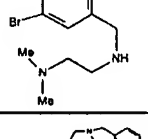
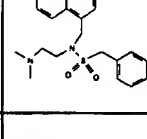
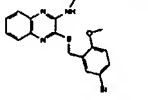
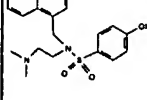
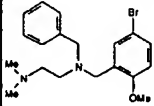
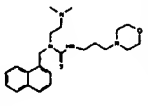
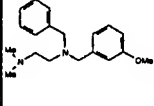
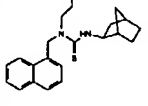
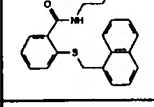
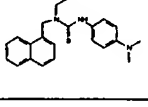
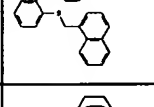
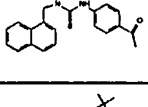
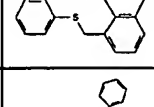
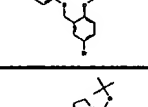
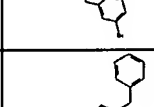
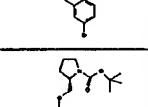
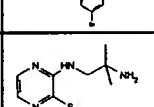
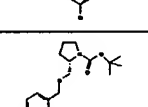
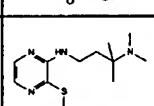
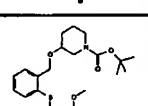
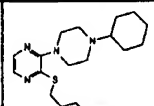
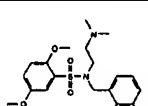


| | | | |
|----|---|---|---|
| WA | C-[1-(2-Naphthalen-1-yl-ethyl)-piperidin-2-yl]-methyl-N-piperidine |  | . |
| WB | 1-[1-(2-Naphthalen-1-yl-ethyl)-piperidin-2-ylmethyl]-1H-pyrrole-2-carbonitrile |  | . |
| WC | 1-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-2-pyrrolidin-1-yl-ethanone |  | . |
| WD | 1-[2-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-ethyl]-piperidine |  | . |
| WE | 3-(5-Bromo-2-methoxy-benzoyloxy)-piperidine |  | . |
| WF | 5-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-2-one |  | . |
| WG | 5-(Naphthalen-1-ylsulfanylmethyl)-1-(2-pyrrolidin-1-yl-ethyl)-pyrrolidin-2-one |  | . |
| WH | 2-[3-(5-Bromo-2-methoxy-benzoyloxy)-pyrrolidin-1-yl]-ethyl-1,N-pyrrolidine |  | . |
| WI | 2-[[[3-Bromo-benzyl]-naphthalen-1-ylmethyl-amino]-methyl]-piperidine-1-carboxylic acid tert-butyl ester |  | . |
| WJ | 4-(2-Methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydroisoquinoline |  | . |
| WK | 4-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydroisoquinoline |  | . |

TABLE 5

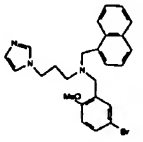
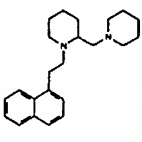
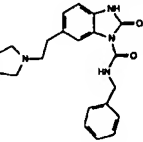
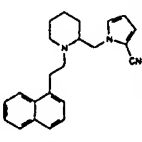
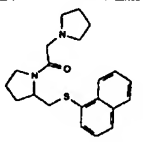
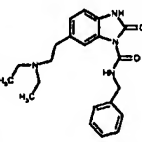
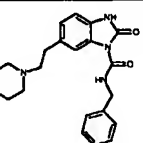
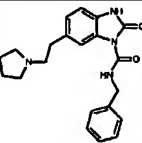
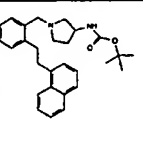
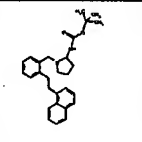
| Salt | Molecular Weight | Structure | Salt | Molecular Weight | Structure |
|---------|------------------|---|--------|------------------|---|
| Parent | 347.5242 |  | Parent | 466.6471 |  |
| Parent | 331.9091 |  | Parent | 508.7277 |  |
| Parent | 333.4453 |  | Parent | 377.3244 |  |
| Parent | 365.4626 |  | Parent | 378.5383 |  |
| Parent | 646.0503 |  | Parent | 406.5921 |  |
| Formate | 513.4192 |  | Parent | 348.4882 |  |
| Formate | 533.4937 |  | Parent | 404.5762 |  |
| Formate | 595.5646 |  | Parent | 312.4552 |  |
| HCl | 525.9799 |  | Parent | 348.4882 |  |

| | | | | | |
|---------|----------|---|---------|----------|---|
| Formate | 530.4901 |  | Parent | 328.4546 |  |
| Formate | 599.6367 |  | Parent | 372.3079 |  |
| Formate | 579.5194 |  | Parent | 377.3244 |  |
| Formate | 590.5457 |  | Parent | 337.2916 |  |
| Formate | 568.4987 |  | Parent | 458.6678 |  |
| Formate | 535.5096 |  | Parent | 353.5078 |  |
| Parent | 561.5456 |  | Parent | 362.4717 |  |
| Formate | 559.5316 |  | Formate | 468.5781 |  |
| Formate | 534.4815 |  | Formate | 527.4406 |  |
| Formate | 507.4559 |  | Formate | 468.5781 |  |

| | | | | | |
|---------|----------|---|---------|----------|---|
| Formate | 493.429 |  | Formate | 502.8609 |  |
| Parent | 591.6153 |  | Formate | 516.8877 |  |
| Parent | 527.5285 |  | Formate | 482.605 |  |
| Formate | 483.4339 |  | Parent | 321.2376 |  |
| Parent | 178.2774 |  | Parent | 454.6122 |  |
| Parent | 426.1942 |  | Parent | 513.4747 |  |
| Parent | 392.2957 |  | Parent | 432.9709 |  |
| Parent | 649.6519 |  | Parent | 467.449 |  |
| Formate | 333.2297 |  | Parent | 382.5267 |  |
| Formate | 595.5646 |  | Parent | 398.5261 |  |

| | | | | | |
|---------|----------|---|--------|----------|---|
| Parent | 377.3244 |  | HCl | 451.0753 |  |
| Parent | 298.4283 |  | HCl | 418.0454 |  |
| Parent | 404.5762 |  | HCl | 443.0552 |  |
| Parent | 447.6446 |  | HCl | 442.024 |  |
| Parent | 402.5603 |  | Parent | 508.4765 |  |
| Parent | 549.5346 |  | Parent | 508.4765 |  |
| Formate | 581.5377 |  | Parent | 522.5034 |  |
| Formate | 443.3691 |  | Parent | 522.5034 |  |
| Formate | 485.4497 |  | Parent | 522.5034 |  |
| Formate | 523.4986 |  | Parent | 428.5524 |  |

| | | | | | |
|---------|----------|--|---------|----------|--|
| Formate | 457.396 | | Parent | 374.528 | |
| Formate | 529.4595 | | Parent | 387.5029 | |
| Formate | 338.4082 | | Parent | 294.4399 | |
| Formate | 340.3808 | | Parent | 353.3024 | |
| Formate | 336.3924 | | HCl | 472.873 | |
| Parent | 293.4118 | | Formate | 467.388 | |
| Parent | 336.4003 | | Parent | 278.3538 | |
| Parent | 318.4619 | | Parent | 282.4289 | |
| Parent | 378.4742 | | Parent | 296.4558 | |
| Parent | 406.528 | | Formate | 443.3855 | |

| | | | | | |
|----------------|----------|---|----------------|----------|---|
| Parent | 464.4051 |  | Parent | 336.5206 |  |
| Parent | 364.4473 |  | Parent | 343.4717 |  |
| Formate | 400.5463 |  | Not Determined | |  |
| Parent | 430.5902 |  | Not Determined | |  |
| Not Determined | |  | Not Determined | |  |

Example 3: cAMP Assay for MC4-R Antagonist Activity**Method**

5 MC4 Receptors are expressed in stably transfected K293 cells. The cells are incubated in DMEM base medium (10% FBS, 1X glutamine, and 0.4 mg/ml G418) at 37°C, in an atmosphere of 6.0% CO₂ and 90% relative humidity. Two days before the experiment, the cells are trypsinized and 200 µl of the cell suspension (138,000 cells/ml) is deposited into 96-well Costar cell culture plates.

10 The test compounds are then dissolved in DMSO creating a 30mM stock solution, which is subsequently diluted to 180, 650, 20, 6.6, 2.2 µM in OPTI-MEM (GIBCO-BRL) media with 50 µM IBMX (isobutylmethylxanthine, Sigma) minutes before the experiment.

 The media is then thoroughly removed from the cell culture plates
15 through a 12-channel straight manifold. 90 µl of OPTI-MEM media with 50 µM IBMX is added to each well (McHale et al. *FEBS Letters* 345 (1994) 147-150). The plate is then placed in an incubator set at 37 °C, 6.0% CO₂ and 90% relative humidity. After 15 minutes of incubation, 90 µl of the test compound solutions (or a control solution of OPTI-MEM and IBMX) are added and the plates are incubated for another 10 minutes.
20 20 µl of the ligand MSH solution in OPTI-MEM is then added. The cell plates are incubated for an additional hour at 37 °C.

 After the incubation, the media mixture is removed by 12-channel straight manifold. 60 µl of 70% ethanol is added to each well. The plates are then placed on a shaker for 30 minutes to extract the cAMP. The amount of cAMP is
25 detected by the cyclic AMP [¹²⁵I] Biotrak SPA screening assay system (Amersham). The system involves adding 50 µl of 1X assay buffer into each well of an OptiPlate-96 (Packard). 50 µl of the tracer solution (cAMP-¹²⁵I) is added into each well. 5 µl of the cAMP extract is added into the mixture, followed by the addition of cAMP antiserum and 50 µl of SPA PVT-antibody binding beads. The plates are then covered with
30 TopSeal-A (Parkard) and incubated at room temperature for up to fifteen hours before being analyzed using a TOPCOUNT machine.

 Compounds O, N, AG, AL, and AM were found to be at least 100 fold more selective for MC4-R than MC1-R, MC3-R and MC5-R.

35

Example 4: In Vivo Assay for MC4-R Antagonist Activity

The following *in vivo* assay was used to test the effects of MC4-R antagonists on mice.

5 Male lean C57BL/6J mice were individually housed in macrolon cages (22 ± 2°C; 12:12 h light/dark cycle with lights off at 6 pm). Tap water and mouse chow diet were given *ad libitum*. Mice were stereotactically implanted with a chronic guide cannula aimed to the third ventricle (intracerebroventricular) one week prior to testing.

It had been previously determined that food deprived lean mice which
10 had been injected with 0.1 nmol of MT II (a MC4-R agonist) prior to refeeding showed decreased feeding response within 1 hour of injection (Figure 1). In previous experiments using peptidic MC4-R antagonists, it has been shown that the decreased feeding response of MT II treated food-deprived mice can be reversed by the intracerebroventricular injection of MC4-R antagonists.

15 In this experiment, food deprived lean mice were injected intracerebroventricularly with either Compound N or Compound O, at a dose of 15 nmol prior to injection of MT II at the dose of 0.05 nmol.

The results of the experiment are shown in Figures 2 and 3. Figure 2 shows that administration of 15 nmol of Compound N partially reverses the effect of the
20 administration of the MC4-R agonist, MT II. Figure 3 shows that administration of Compound O did not significantly effect the food intake of mice treated with MT II.

Example 5: cAMP Assay for MC Receptor Agonist Activity (cAMP Assay)

The cAMP assay identifies compounds which have agonist activity
25 against MC receptors. It is used to identify the selectivity of agonist which selectively antagonize receptors of interest. The following method is outlined for MC4-R, but corresponding procedures were used for the other MC receptors, MC1-R, MC3-R, and MC5-R.

30 Method

MC4 Receptors are expressed in stably transfected HEK293 cells. The cells are incubated in DMEM base medium (10% FBS, 1X glutamine, and 0.4 mg/ml G418) at 37°C, in an atmosphere of 6.0% CO₂ and 90% relative humidity. Two days before the experiment, the cells are trypsinized and 200 µl of the cell suspension
35 (138,000 cells/ml) is deposited into 96-well Costar cell culture plates.

The test compounds are then dissolved in DMSO creating a 30mM stock solution, which is subsequently diluted to 180, 650, 20, 6.6, 2.2 μ M in OPTI-MEM (GIBCO-BRL) media with 50 μ M IBMX (isobutylmethylxanthine, Sigma) minutes before the experiment.

5 The media is then thoroughly removed from the cell culture plates through a 12-channel straight manifold. 90 μ l of OPTI-MEM media with 50 μ M IBMX is added to each well (McHale et al. *FEBS Letters* 345 (1994) 147-150). The plate is then placed in an incubator set at 37 °C, 6.0% CO₂ and 90% relative humidity. After 15 minutes of incubation, 90 μ l of the test compound solutions (or a control solution of
10 OPTI-MEM and IBMX) are added and the plates are incubated for another 10 minutes. 20 μ l of the ligand MSH solution in OPTI-MEM is then added. The cell plates are incubated for an additional hour at 37 °C.

 After the incubation, the media mixture is removed by 12-channel straight manifold. 60 μ l of 70% ethanol is added to each well. The plates are then
15 placed on a shaker for 30 minutes to extract the cAMP. The amount of cAMP is detected by the cyclic AMP [¹²⁵I] Biotrak SPA screening assay system (Amersham). The system involves adding 50 μ l of 1X assay buffer into each well of an OptiPlate-96 (Packard). 50 μ l of the tracer solution (cAMP-¹²⁵I) is added into each well. 5 μ l of the cAMP extract is added into the mixture, followed by the addition of cAMP antiserum
20 and 50 μ l of SPA PVT-antibody binding beads. The plates are then covered with TopSeal-A (Packard) and incubated at room temperature for up to fifteen hours before being analyzed using a TOPCOUNT machine.

INCORPORATION BY REFERENCE

25 The entire contents of all references and patents cited herein are hereby incorporated by reference. The entire contents of U.S. Patent 5,908,609 and all its references also expressly incorporated herein.

EQUIVALENTS

30 Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments and methods described herein. Such equivalents are intended to be encompassed by the scope of the following claims.

CLAIMS

1. A method for treating a MC4-R associated state in a mammal comprising administering an effective amount of a MC4-R binding compound to a mammal, such
5 that the MC4-R associated state is treated, wherein said compound is of the formula (I):



wherein

- 10 B is an anchor moiety;
Z is a central moiety; and
E is a MC4-R interacting moiety.

2. The method of claim 1, wherein said compound binds to the MC4-R with an IC_{50} of about 5 μM or less.

- 15 3. The method of claim 2, wherein said compound binds to the MC4-R with an IC_{50} of about 1 μM or less.

4. The method of claim 3, wherein said compound binds to the MC4-R with an IC_{50}
20 of about 0.5 μM or less.

5. The method of claim 4, wherein said compound binds to the MC4-R with an IC_{50} of about 0.1 μM or less.

- 25 6. The method of claim 5, wherein said compound binds to the MC4-R with an IC_{50} of about 0.05 μM or less.

7. The method of claim 6, wherein said compound binds to the MC4-R with an IC_{50}
30 of about 0.03 μM or less.

8. The method of claim 1, wherein said compound is an antagonist of the MC4-R.

9. The method of claim 1, wherein said compound is an agonist of the MC4-R.

- 35 10. The method of claim 1, wherein said effective amount is effective to treat a disorder associated with pigmentation, bones or weight loss.

11. The method of claim 10, wherein said effective amount is effective to treat a disorder associated with weight loss.

12. The method of claim 11, wherein said weight loss is a result of anorexia nervosa,
5 old age, cancer cachexia, or HIV cachexia.

13. The method of claim 1, wherein said mammal is a human.

14. A method for treating an MC4-R associated state in a mammal comprising
10 administering an effective amount of a MC4-R binding compound to a mammal, such that the MC4-R associated state is treated, wherein said compound is of the formula (III):



15

wherein:

B is an anchor moiety;

L₁ and L₂ are linking moieties;

A is a cyclic moiety; and

20

E is a MC4-R interacting moiety,

15. The method of claim 14, wherein B is substituted or unsubstituted alkyl, alkenyl, alkynyl, aryl, or heterocyclic.

25 16. The method of claim 15, wherein B is aryl.

17. The method of claim 16, wherein B is carbocyclic.

18. The method of claim 17, wherein B is phenyl.

30

19. The method of claim 18, wherein B is substituted with at least one substituent, wherein each substituent is independently selected from the group consisting of halogens, alkoxy, hydroxy, alkylcarbonyl, cyano, nitro, thioether, thioalkyl, thiol, alkyl, alkenyl, alkynyl, aryl, arylalkynyl, and arylalkyl.

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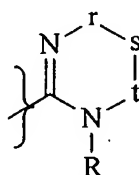
20. The method of claim 19, wherein B is substituted with at least one halogen.

21. The method of claim 19, wherein B is substituted with at least one alkoxy group.

22. The method of claim 20, wherein B is 2-alkoxy-5-bromo phenyl.
23. The method of claim 22, wherein B is 2-methoxy-5-bromo phenyl.
- 5 24. The method of claim 19, wherein B is substituted with at least one alkyl group.
25. The method of claim 16, wherein B comprises more than one aromatic ring.
- 10 26. The method of claim 25, wherein B is substituted or unsubstituted naphthyl, fluorene, anthracene, or biphenyl.
27. The method of claim 26, wherein B is substituted or unsubstituted naphthyl.
- 15 28. The method of claim 26, wherein B is substituted with one or more substituents selected from the group consisting of halogens, alkoxy, hydroxy, alkylcarbonyl, cyano, nitro, thiol, thioether, thioalkyl, alkyl, alkenyl, alkynyl, aryl, arylalkynyl, and arylalkyl.
29. The method of claim 15, wherein B comprises a heterocycle.
- 20 30. The method of claim 29, where B comprises a substituted heterocycle.
31. The method of claim 29, wherein B is substituted or unsubstituted furanyl, imidazolyl, benzothiophenyl, benzofuranyl, quinoliny, isoquinoliny, benzodioxanyl, benzoxazolyl, benzothiazolyl, methylenedioxyphenyl, ethylenedioxyphenyl, piperidiny, 25 indolyl, thienyl, pyrimidyl, pyrazinyl, purinyl, or deazapurinyl.
32. The method of claim 14, wherein L_1 is a covalent bond or a substituted or unsubstituted chain of one to six atoms.
- 30 33. The method of claim 32, wherein said chain comprises a carbon atom and at least one other atom selected from the group consisting of carbon, sulfur, oxygen, or nitrogen.
34. The method of claim 33, wherein said chain comprises a sulfur atom.
- 35 35. The method of claim 33, wherein said chain comprises an oxygen atom.
36. The method of claim 33, wherein said chain comprises two carbon atoms.

37. The method of claim 14, wherein A is substituted or unsubstituted phenyl, heteroaryl, or bicyclic.
- 5 38. The method of claim 37, wherein A is unsubstituted phenyl.
39. The method of claim 37, wherein A is substituted phenyl.
40. The method of claim 39, wherein A is substituted with one or more substituents
10 selected from the group consisting hydroxy, chlorine, fluorine, bromine, iodine, amino, cyano, alkoxy, aryl, and alkyl.
41. The method of claim 40, wherein A is substituted with chlorine.
- 15 42. The method of claim 40, wherein A is substituted with fluorine.
43. The method of claim 40, wherein said alkyl group is methyl, trifluoromethyl, ethyl, propyl, or butyl.
- 20 44. The method of claim 40, wherein said alkoxy group is methoxy, ethoxy, propoxy, or butoxy.
45. The method of claim 37, wherein A is heteroaryl and selected from the group consisting of pyrimidyl, pyrazinyl, thienyl, pyrrolyl, imidazolyl, and quinoxaliny.
- 25 46. The method of claim 37, wherein A is bicyclic and selected from the group consisting of methylenedioxyphenyl, isoindole, indole, and indan.
47. The method of claim 14, wherein L₂ is selected from the group consisting of a
30 covalent bond, a carbonyl moiety, a thiocarbonyl moiety or C₁-C₆ branched or unbranched alkyl, wherein one, two or three of the carbons are optionally replaced with any combination of substituted or unsubstituted oxygen, sulfur and nitrogen atoms.
48. The method of claim 47, wherein L₂ is a covalent bond.
- 35 49. The method of claim 14, wherein said MC₄-R interacting moiety is a substituted or unsubstituted amino group, alkyl, cyano, guanidino, amidino, or a heterocyclic moiety.

50. The method of claim 49, wherein E is dialkylamino.
51. The method of claim 49, wherein E is heterocyclic.
52. The method of claim 51, wherein E contains a nitrogen atom.
53. The method of claim 52, wherein E is substituted or unsubstituted piprazinyl, imidazolyl, imidazoliny, imidoazopyridinyl, pyrroloimidazolyl, pyrrolyl, azetidiny, azapanyl, diazapanyl, pyrimidinyl, pyridinyl, morpholinyl, or piperidinyl.
54. The method of claim 51, wherein E is multicyclic.
55. The method of claim 54, wherein E is a bridged or fused ring.
56. The method of claim 52, wherein E is of the formula (XIII):



(XIII)

wherein

- r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;
- t is CH, CH₂, CHR³, CR³R⁴, or H;
- s is CH, CH₂, alkenyl, CHR⁵, CR⁵R⁶, or absent;
- R is hydrogen, alkyl, alkenyl, arylalkyl, alkoxycarbonyl, arylcarbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to A, B, L₁, L₂, R¹, R², R³, R⁴, R⁵, or R⁶ to form a ring; and
- R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioalkyl, thioether, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, aryl, hydroxyl, nitro, amino, cyano, optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

57. The method of claim 56, wherein each of r, s and t are CH₂.
58. The method of claim 56, wherein R is H, alkyl, arylcarbonyl, alkoxycarbonyl, alkylcarbonyl, or arylalkylcarbonyl.

59. The method of claim 58, wherein R is selected from the group consisting of methyl, ethyl, and propyl.

60. The method of claim 56, wherein r is a covalent bond.

5

61. The method of claim 14, wherein said compound is an MC4-R antagonist.

62. The method of claim 14, wherein said effective amount is effective to treat a disorder associated with weight loss or bones.

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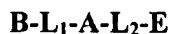
63. The method of claim 62, wherein said weight loss is a result of anorexia nervosa, old age, cancer cachexia, or HIV cachexia.

64. The method of claim 14, wherein said mammal is a human.

15

65. A method for treating an MC4-R associated state in a mammal comprising administering an effective amount of a MC4-R binding compound to said mammal, such that the MC4-R associated state is treated, wherein said compound is an MC4-R antagonist, and is of the formula (III):

20



(III)

wherein

B is substituted or unsubstituted biaryl, unsubstituted or substituted heterocyclic, or unsubstituted or substituted phenyl, wherein one or more of said substituents are
25 halogens, hydroxy, alkyl, alkynyl, alkoxy, aryl, amino, cyano, or nitro;

L₁ is a covalent bond, C₁-C₆ branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms;

L₂ is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl;

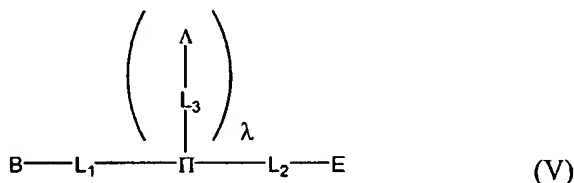
30 E is substituted or unsubstituted alkyl, amino, amidino, guanidino, heterocyclic, or aryl, wherein said substituents are amino, arylalkyl, aminoalkyl, alkyl, aryl, alkenyl, or alkynyl; and

A is a substituted or unsubstituted phenyl, heteroaryl, cycloalkyl, or biaryl, and pharmaceutically acceptable salts thereof.

35

66. The method of claim 65, wherein B is substituted or unsubstituted phenyl or naphthyl.

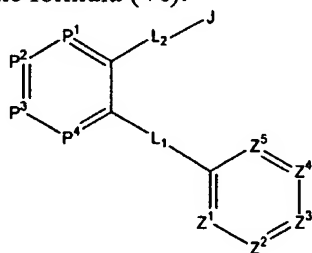
67. The method of claim 65, wherein B is phenyl substituted with at least one halogen or alkoxy substituent.
68. The method of claim 65, wherein L_1 is a thioether or an ether.
- 5 69. The method of claim 65, wherein L_2 is a covalent bond.
70. The method of claim 65, wherein A is phenyl.
- 10 71. The method of claim 65, wherein A is heteroaryl.
72. The method of claim 65, wherein E is heterocyclic.
73. A method for treating an MC4-R associated state in a mammal comprising
 15 administering an effective amount of a MC4-R binding compound to said mammal, such that the MC4-R associated state is treated, wherein said compound is an MC4-R antagonist, and is of the formula (V):



- 20 B is substituted or unsubstituted biaryl, unsubstituted or substituted heterocyclic, or unsubstituted or substituted phenyl, wherein one or more of said substituents are halogens, hydroxy, alkyl, alkynyl, alkoxy, aryl, amino, cyano, or nitro;
- L_1 is a covalent bond, C_1 - C_6 branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms;
- 25 L_2 is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl;
- E is substituted or unsubstituted alkyl, amino, amidino, guanidino, heterocyclic, or aryl, wherein said substituents are amino, arylalkyl, aminoalkyl, alkyl, aryl, alkenyl, or alkynyl;
- 30 Π is a covalent bond, a carbon atom, a nitrogen atom, heterocyclic, alkyl, cycloalkyl, or aryl;
- L_3 is a covalent bond, C_1 - C_6 branched, unbranched or cyclic alkyl, wherein one, two or three of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms, carbonyl, aminocarbonyl, aminocarbonylamino, aminocarbonyloxy, or
 35 aminothiocarbonyl; and

Λ is heterocyclic, aryl, alkoxy, amino, alkyl, alkenyl, alkynyl, or hydrogen; and λ is 0, 1 or 2, and pharmaceutically acceptable salts thereof.

74. A method for treating an MC4-R associated state in a mammal comprising
 5 administering an effective amount of a MC4-R binding compound to a mammal, such that the MC4-R associated state is treated, wherein said compound is an MC4-R antagonist, and is of the formula (VI):



(VI)

wherein

- 10 P¹, P², P³, and P⁴ are optionally substituted carbon, sulfur, or nitrogen, and wherein one of P¹, P², P³, and P⁴ may represent a covalent bond;
 Z¹, Z², Z³, Z⁴, and Z⁵ are optionally substituted carbon or nitrogen;
 L¹ is a covalent bond, C₁-C₆ branched or unbranched alkyl, wherein one or two of the carbons are optionally replaced with oxygen, sulfur or nitrogen atoms;
 15 L₂ is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl;
 L₂ is a covalent bond, substituted or unsubstituted amino, ether, thioether, or alkyl; and
 J is an unsubstituted or substituted nitrogen containing heterocycle or a
 20 substituted or unsubstituted amino group, and pharmaceutically acceptable salts thereof.

75. The method of claim 74, wherein P¹, P², P³, and P⁴ are each substituted or unsubstituted carbon.

- 25 76. The method of claim 74, wherein P⁴ is sulfur, P¹ is a covalent bond, and P² and P³ are substituted or unsubstituted carbon.

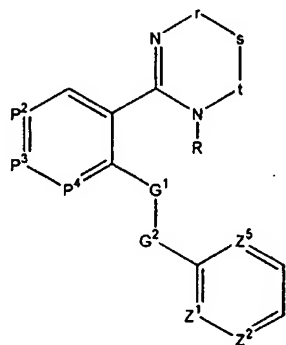
77. The method of claim 75, wherein P¹ and P³ are CH.

- 30 78. The method of claim 75, wherein P² and P⁴ are each independently CH, CF, CCl, CBr, Cl, C-alkyl, C-alkoxy, or C-aryl.

79. The method of claim 78, wherein P² is CH.

80. The method of claim 78, wherein P^4 is CCl or CF.
81. The method of claim 74, wherein Z^3 and Z^4 are each CH.
- 5 82. The method of claim 74, wherein Z^1 is CH, or covalently linked to Z^2 to form a naphthyl ring.
83. The method of claim 74, wherein Z^2 is CH, C-(C \equiv CH), CCl, CBr, Cl, CF, or
10 covalently linked to Z^1 to form a naphthyl ring.
84. The method of claim 83, wherein Z^2 is CBr.
85. The method of claim 74, wherein Z^5 is CH, C-alkoxy, or COH.
- 15 86. The method of claim 85, wherein Z^5 is C-OMe.
87. The method of claim 74, wherein L^2 is a covalent bond.
- 20 88. The method of claim 74, wherein J is substituted or unsubstituted imidazolyl, imidazoliny, piprazinyl, imidoazopyridinyl, pyrroloimidazolyl, pyrrolyl, azetidiny, azapanyl, diazapanyl, pyrimidinyl, pyridinyl, morpholinyl, or piperidinyl.
89. The method of claim 74, wherein J is a substituted or unsubstituted fused ring or
25 bridged heterocycle.
90. The method of claim 74, wherein said MC4-R binding compound is of the formula (IX):

30



(IX)

wherein:

P² is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or a covalent bond;

5 P³ is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, or Cl;

P⁴ is CH, CCl, CBr, CF, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or a sulfur atom;

G¹ and G² are each independently CH₂, S, or O;

r is a covalent bond or CH₂;

10 t is CH₂, CHR³, or CR³R⁴;

s is CH₂, CHR⁵ or CR⁵R⁶;

R is hydrogen, alkyl, alkoxycarbonyl, or alkylcarbonyl;

Z¹ is CH, or covalently linked to Z² to form a naphthyl ring;

15 Z² is CH, C-(C≡CH), CCl, CBr, Cl, CF, or covalently linked to Z¹ to form a naphthyl ring;

Z⁵ is CH, or C-alkoxy;

R³, R⁴, R⁵, and R⁶ are methyl, ethyl, hydroxyl, alkoxy, halogen, cyano, nitro, or amino, or pharmaceutically acceptable salts thereof.

20 91. The method of claim 90, wherein Z¹ is CH, Z² is CBr and Z⁵ is C-OMe.

92. The method of claim 90, wherein P² is CH.

93. The method of claim 90, wherein P⁴ is CCl or CF.

25

94. The method of claim 90, wherein G¹ and G² are each CH₂.

95. The method of claim 90, wherein G¹ and G² together are -CH₂-S- or -S-CH₂-.

30 96. The method of claim 90, wherein Z¹ and Z² are linked to form a naphthyl ring.

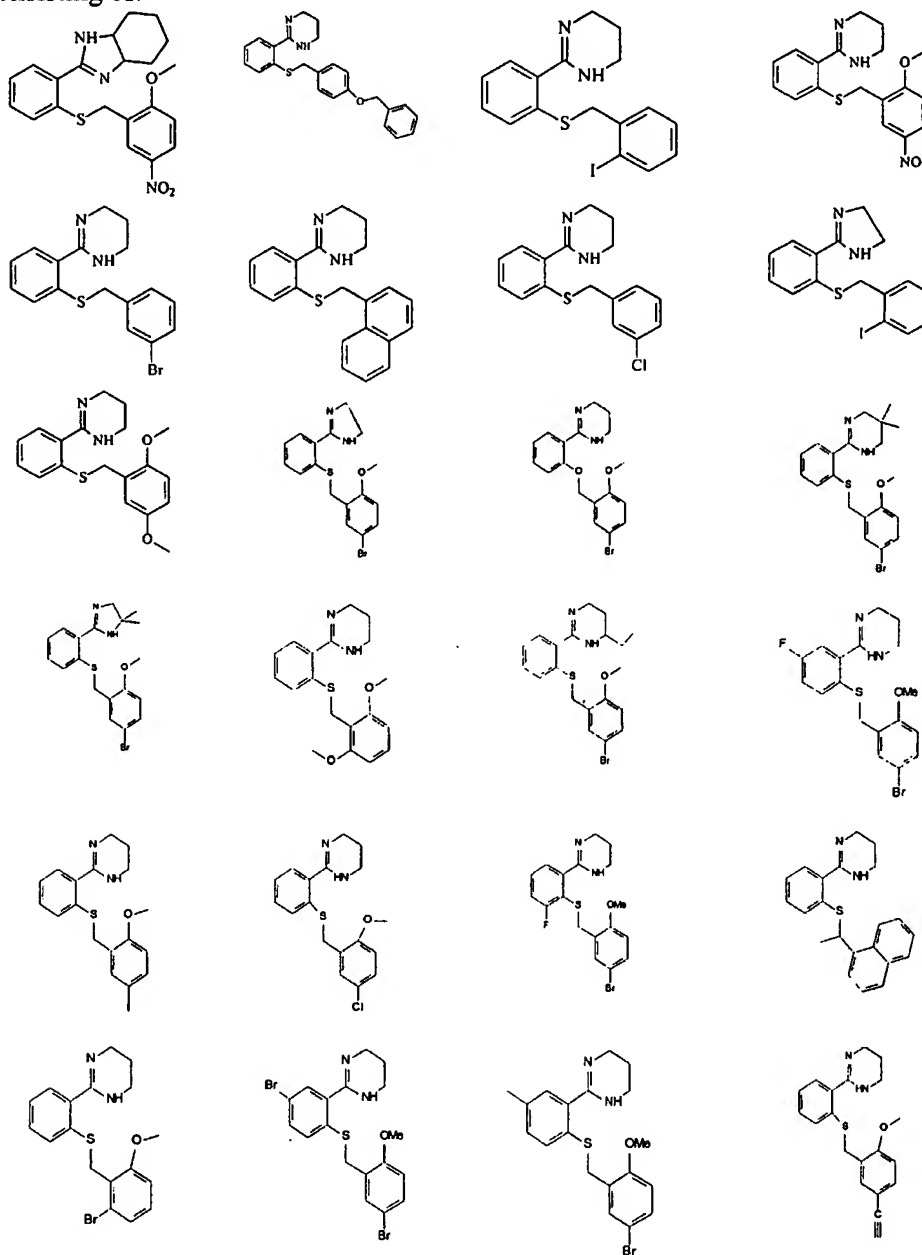
97. The method of claim 90, wherein r is a covalent bond; s is CR⁵R⁶; and t is CR³R⁴, wherein R³, R⁴, R⁵, and R⁶ are each independently hydrogen or alkyl.

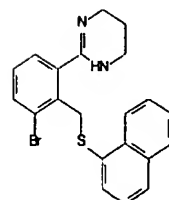
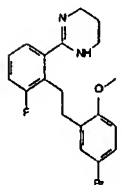
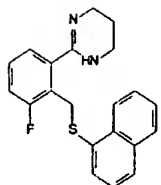
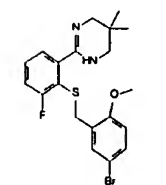
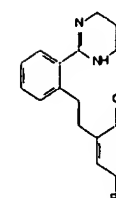
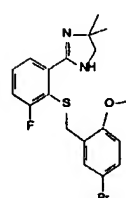
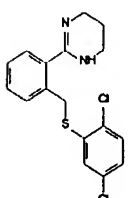
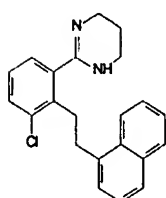
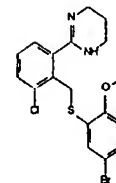
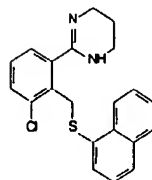
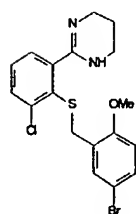
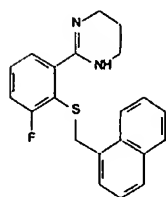
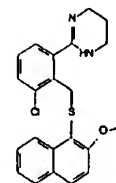
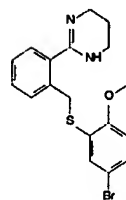
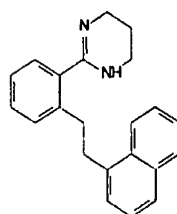
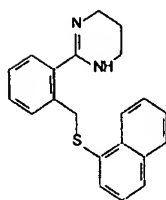
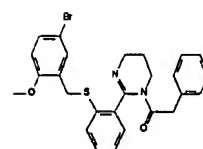
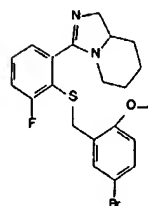
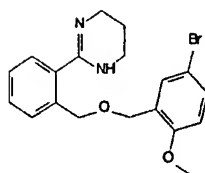
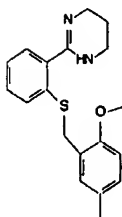
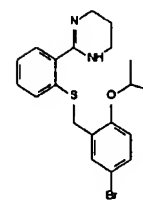
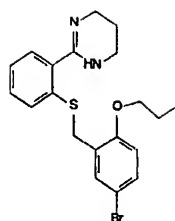
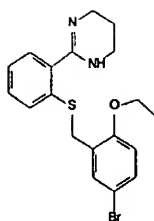
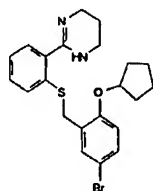
35 98. The method of claim 90, wherein R is hydrogen.

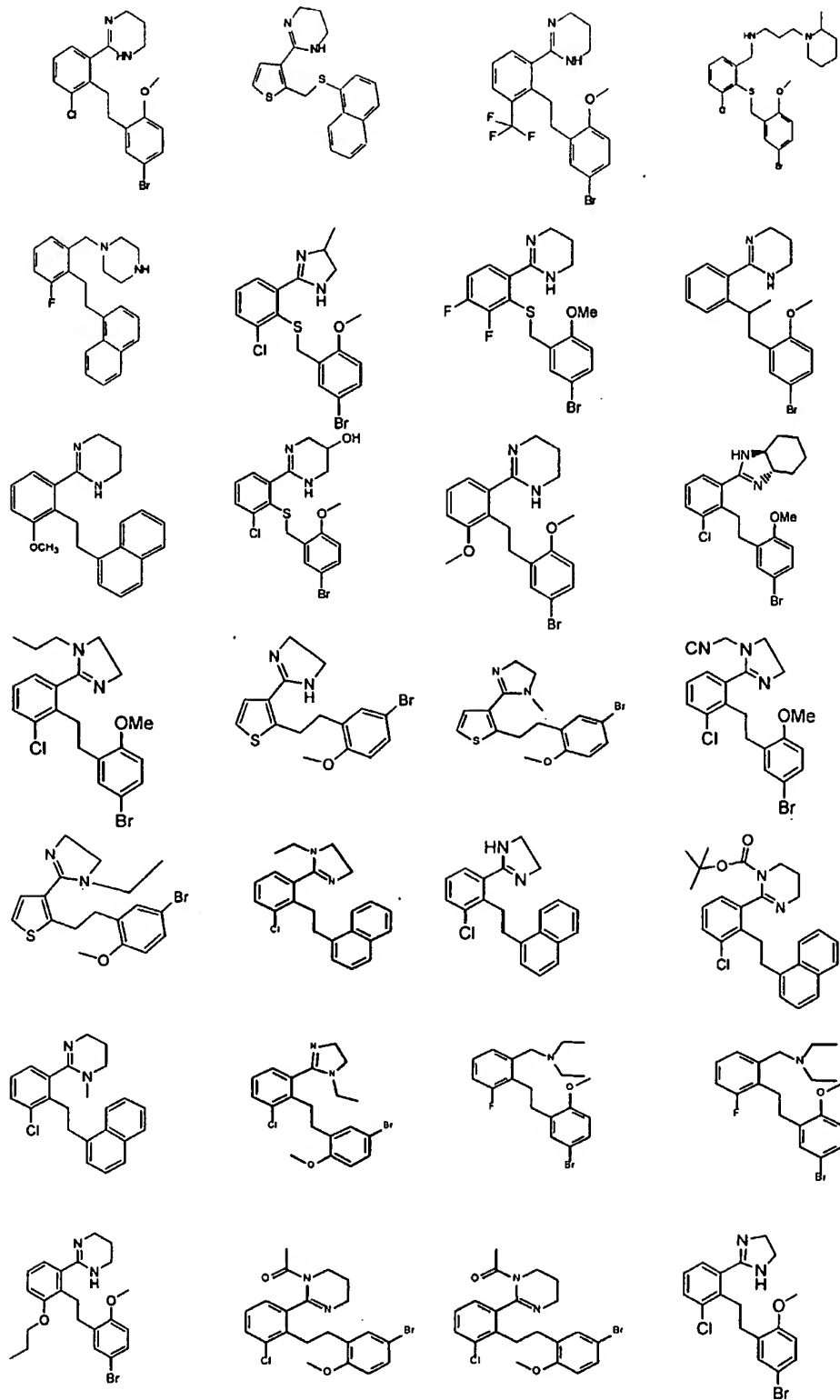
99. The method of claim 90, wherein R is alkyl.

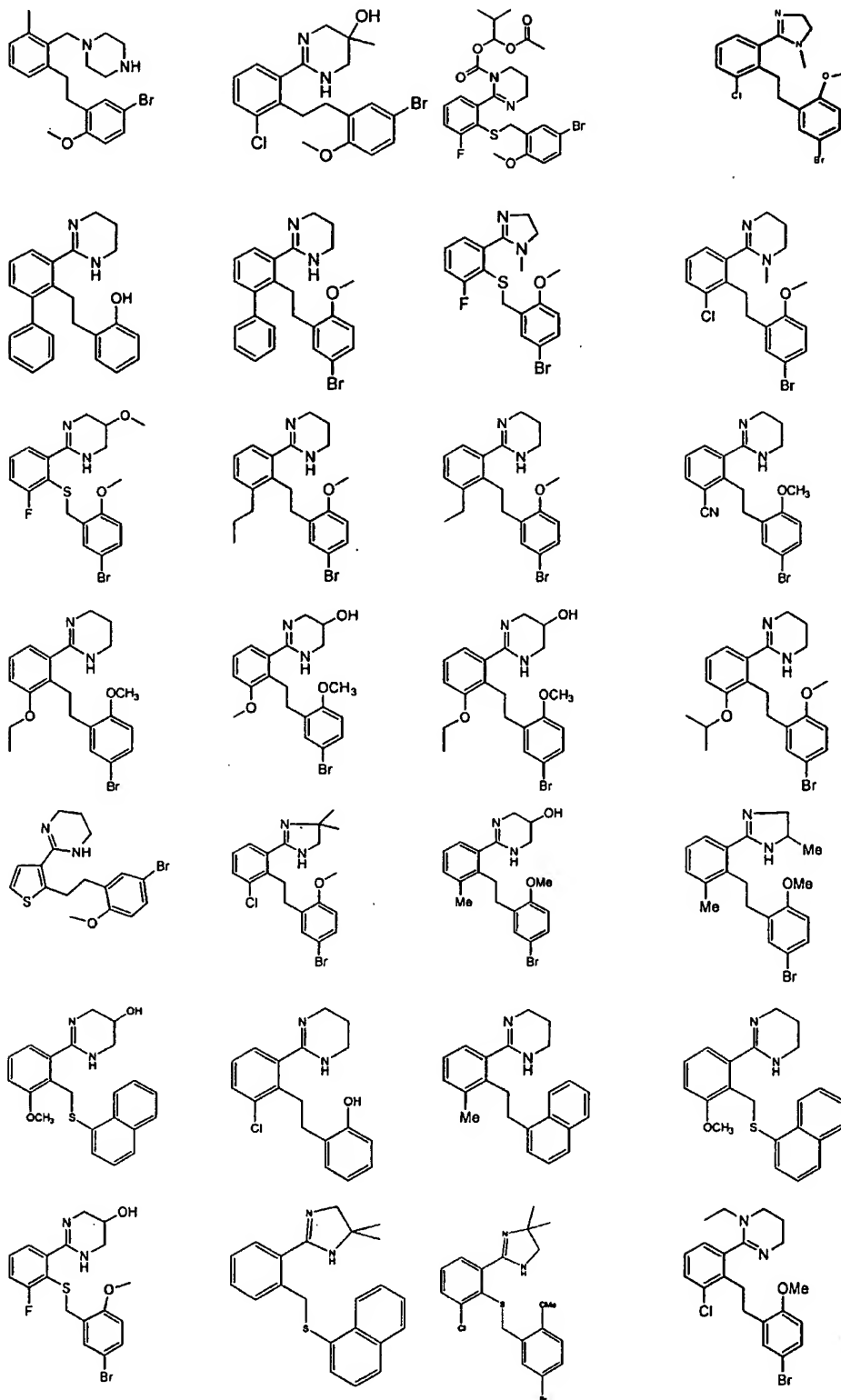
100. The method of claim 99, wherein R is methyl, ethyl, propyl or butyl.

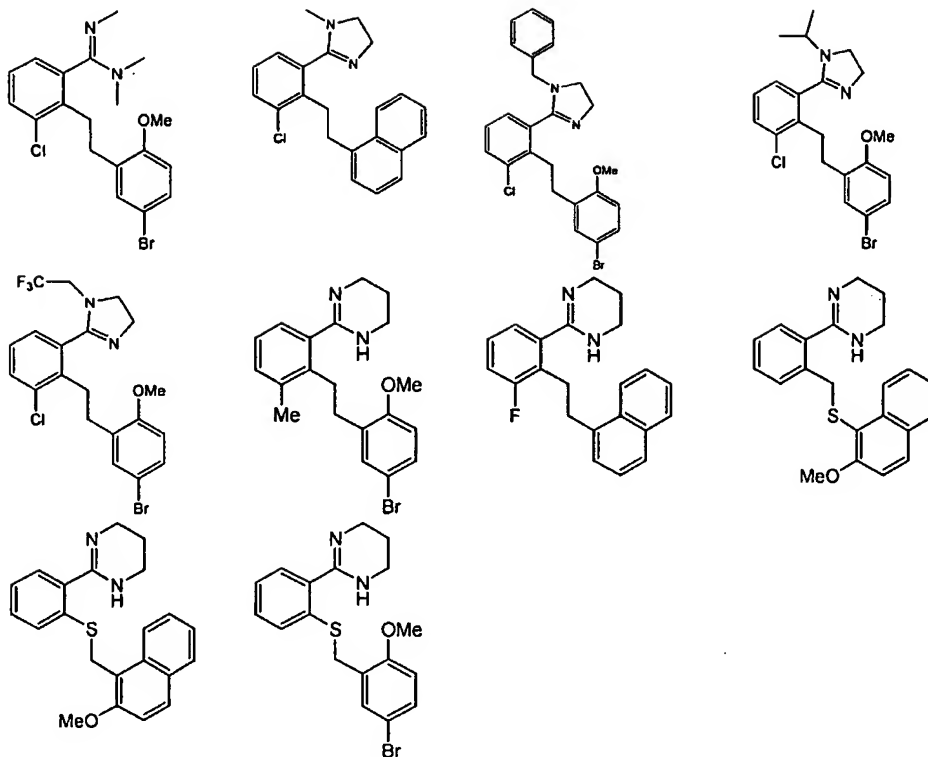
101. The method of claim 74, wherein said compound is selected from the group consisting of:











102. The method of claim 65, wherein said compound is selected from the group consisting of: 2-[2-(4-benzyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 5 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,5-dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 10 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[2-(2-methoxy-5-nitro-benzyloxy)-phenyl]-1,4,5,6-tetrahydropyrimidine;
 2-[2-(2-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 15 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
 2-{2-[2-(2-methoxy-naphthalen-1-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
 2-[2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
 2-{2-[2-(2-methyl-naphthalen-1-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
 20 2-{2-[2-(2,3-dihydro-benzo[1,4]dioxin-5-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;

- 2-[2-(2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
 2-(2-Benzylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-(2-Pentadecylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-(2-Cyclohexylmethylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 5 2-[2-(2-Methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-Nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3,5-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(4-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 10 2-[2-(2-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,4-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3,5-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-nitro-benzoyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 15 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-(2-Benzylsulfanyl-phenyl)-4,5-dihydro-1H-imidazole;
 2-[2-(2,6-Difluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(Naphthalen-1-ylmethoxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 20 1-{2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-
 ethanone;
 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-
 benzoimidazole;
 2-[2-(2-Iodo-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
 25 2-[2-(2,5-Dimethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 4-[2-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-quinoline;
 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-pyridin-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Cyclopentylloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 30 2-[2-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 pyrimidine;
 2-[2-(6-Methoxy-2,3-dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-
 tetrahydro-pyrimidine;
 2-[2-(5-fluoro-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 35 1-Methyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[2-(5-Bromo-2-methoxy-benzoyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(Naphthalen-1-ylloxymethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 5 2-[2-(2,6-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2-Bromo-6-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[4-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2-Bromo-5-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(Biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Chloro-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2-Methoxy-5-thiophen-3-yl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(Biphenyl-2-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-(5-Iodo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 25 2-[2-(4,4'-Dimethoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(9H-Fluoren-9-ylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(3'-Chloro-4'-fluoro-4-methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 30 2-[2-(1-Naphthalen-1-yl-ethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-4,5-dihydro-1H-imidazole;
2-(2-Benzhydrylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(2'-Fluoro-4"-methoxy-[1,1';4',1"]terphenyl-3"-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 35 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzamidine;
2-[4-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Ethynyl-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(5-Bromo-2-cyclopentyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-ethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-propoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperazine;
- C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-morpholin-2-yl}-methylamine;
- 2-[2-(2-Methoxy-5-methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-dimethyl-amine;
- 2-[2-(5-Bromo-2-isopropoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Ethoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Propoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-benzonitrile;
- 1-{4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-phenyl}-ethanone;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 20 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;
- C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-methylamine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
- 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
- 25 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,5,6,7,8a-hexahydro-imidazo[1,5-a]pyridine;
- 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole;
- 2-[2-(Benzo[b]thiophen-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 30 2-[3-Fluoro-2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-(Naphthalen-1-ylmethylsulfanyl)-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 35 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-3-methyl-butan-1-one;
- 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-2-phenyl-ethanone;

- 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyridin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 N-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-guanidine;
 2-[2-(2-Isopropoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(2-Cyclopentyloxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 (5-Bromo-2-methoxy-benzyl)-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[2-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(6-Bromo-2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[3-Chloro-2-(2-methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[1-(2-Naphthalen-1-yl-ethyl)-1H-pyrrol-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 (5-Bromo-2-methoxy-benzyl)-methyl-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine;
- 25 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamine;
 2-[2-(2-Chloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Bromo-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-(2-o-Tolylsulfanylmethyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,5-Dichloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 30 2-(3-Amino-propylamino)-6-(5-bromo-2-methoxy-benzylsulfanyl)-benzonitrile;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;
 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-morpholine;
 3'-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl;
- 35 2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-piperazin-1-yl-6,7-dihydro-quinoxaline;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;
 C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-methylamine;

- 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-pyrrolidin-3-ylamine;
 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-pyrrolidin-3-ylamine;
 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
 C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-morpholin-3-yl}-
 5 methylamine;
 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-azetidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ol;
 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl
 10 ester;
 [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-
 bicyclo[2.2.2]oct-3-yl ester;
 [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-
 ethyl ester;
 15 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-2-yl}-
 methanol;
 4-tert-Butyl-N-naphthalen-1-ylmethyl-N-(2-piperidin-1-yl-ethyl)-benzamide;
 N,N-Dimethyl-N'-naphthalen-2-ylmethyl-N'-naphthalen-1-ylmethyl-propane-1,3-
 diamine;
 20 N-(5-Bromo-2-methoxy-benzyl)-N',N'-dimethyl-N-naphthalen-1-ylmethyl-propane-1,3-
 diamine;
 1-Naphthalen-1-ylmethyl-3-phenethyl-1-(2-piperidin-1-yl-ethyl)-thiourea;
 3-(4-Dimethylamino-phenyl)-1-(3-dimethylamino-propyl)-1-naphthalen-1-ylmethyl-
 thiourea;
 25 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzylamino]-piperidine-1-
 carboxylic acid ethyl ester;
 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethylamine;
 Naphthalene-2-sulfonic acid (2-dimethylamino-ethyl)-naphthalen-1-ylmethyl-amide;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-2-methoxymethyl-
 30 pyrrolidine;
 (2-Hexyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-pyrrolidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-piperidine;
 35 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-propan-1-ol;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-3-methyl-butan-1-ol;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ol;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-2-yl}-methanol;

- {1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-ethyl-N-pyrrolidine;
 N-pyrrolyl-[1-(2-naphthalen-1-yl-ethyl)-pyrrolidin-2-ylmethyl]-amine;
 1-(2-Naphthalen-1-yl-ethyl)-piperidine-2-carboxylic acid methyl ester;
 5 (3-Bromo-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-amine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-piperidine;
 (5-Bromo-2-methoxy-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-amine;
 (1-Ethyl-pyrrolidin-2-ylmethyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;
 10 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
 (3-Bromo-benzyl)-(3-imidazol-1-yl-propyl)-naphthalen-1-ylmethyl-amine;
 (3-Imidazol-1-yl-propyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;
 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester;
 15 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-dimethylamino-ethyl ester;
 1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-amine;
 1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 20 N,N-Dimethyl-N'-(2-naphthalen-1-yl-ethyl)-N'-naphthalen-1-ylmethyl-ethane-1,2-diamine;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 25 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 {1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 {1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperidin-2-yl}-methanol;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 30 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-pyrrolidin-3-ylamine;
 1-Phenyl-3-piperazin-1-yl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(4-Methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 35 2-[2-(2-Methoxy-5-phenylethynyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[3-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2,5-Dimethoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(4-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-(Naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-
- 15 pyrimidine;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Bromo-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1,4,5,6-tetrahydro-
- 20 pyrimidine;
- 2-[2-(2-Methoxy-5-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[4-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-trifluoromethyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Naphthalen-1-yl-ethyl)-3-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(6-Fluoro-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidin-2-yl}-methanol;
- 30 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-[3-(2-methyl-piperidin-1-yl)-propyl]-amine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ylamine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperazine;
- 35 5,5-Dimethyl-2-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 5 3-(2-Naphthalen-1-yl-ethyl)-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
- Amino-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-acetonitrile;
- 1-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethane-1,2-diamine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 10 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-1-methyl-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-(5-Bromo-2-methoxy benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Methoxy-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-chloro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
- 30 2-[2-(1-Methyl-2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 3-(5-Bromo-2-methoxy-benzylsulfanyl)-2-fluoro-4-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 35 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;

- 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-fluoro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
5 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-Chloro-6-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-ethyl}-phenol;
10 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-5-methyl-4,5-dihydro-1H-imidazole;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
15 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,4-dimethyl-4,5-dihydro-1H-imidazole;
20 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-4-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
4,4-Dimethyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-4,5-dihydro-oxazole;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-4-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
25 2-[5-(5-Bromo-2-methoxy-benzyl)-2-methyl-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
30 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
35 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 5 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-benzonitrile;
- 2-{3-Benzoyloxy-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-butyl-phenyl}-1,4,5,6-tetrahydro-
- 10 pyrimidine;
- 2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-8-chloro-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-
- 20 pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isobutoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5-methoxy-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-
- 30 imidazole;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
- 2-{2-[3-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-biphenyl-2-yl]-ethyl}-phenol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-4,5-dihydro-
- 35 1H-imidazole;
- N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methoxy-benzamide;
- N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzamide;

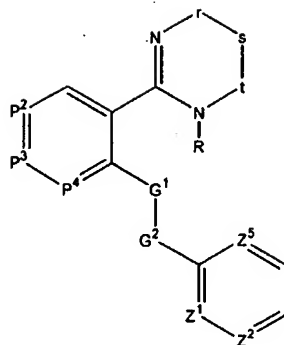
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-2-methyl-propyl ester;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 5 3-(5-Bromo-2-methoxy-phenyl)-5-chloro-3,4-dihydro-isoquinolin-1-ylamine;
 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(4-methoxy-benzyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5-methyl-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 10 2-[(5-Bromo-2-methoxy-phenyl)-(3-piperidin-1-yl-propylamino)-methyl]-3-chloro-6-methyl-phenol;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperidine;
- 15 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-diethyl-amine;
 3-(5-Bromo-2-methoxy-phenyl)-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
- 20 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-methanol;
- 25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
- 30 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 35 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;

- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidin-2-yl)-
 methanol;
 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-
 5 benzamide;
 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
 10 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-
 imidazole;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-
 methanol;
 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-
 pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
 20 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-
 pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
 25 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-
 pyrimidin-1-yl)-ethanone;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
 30 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-
 benzamide;
 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-4,5-dihydro-1H-
 imidazole;
 35 {2-[3-(5-Bromo-2-methoxy-phenyl)-3,4-dihydro-1H-isoquinolin-2-yl]-ethyl}-diethyl-
 amine;
 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-
 imidazol-1-yl)-ethanone;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester;
- 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazol-1-yl)-2,2-dimethyl-propan-1-one;
- 1-(5-Bromo-2-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
- 10 1-(2-Methoxy-benzyl)-2-methyl-2,3-dihydro-1H-isoindole;
- 2-Methyl-1-naphthalen-1-ylmethyl-2,3-dihydro-1H-isoindole;
- 1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-2,2-dimethyl-propan-1-one;
- {2-[1-(5-Bromo-2-methoxy-benzyl)-1,3-dihydro-isoindol-2-yl]-ethyl}-diethyl-amine;
- 15 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid tert-butyl ester;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 20 1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-ethanone;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester;
- 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
- 25 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
- 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-N-(3-formylamino-propyl)-6-methyl-benzamide;
- 30 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-ethyl-4,5-dihydro-1H-imidazole;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-2,2-dimethyl-propan-1-one;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-
- 35 pyrimidine-1-carboxylic acid isobutyl ester;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isocyanomethyl-4,5-dihydro-1H-imidazole;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-methyl-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-ethyl-4,5-dihydro-1H-imidazole;
- 5 3-(5-Bromo-2-methoxy-benzyl)-2-methyl-2,3-dihydro-isoindol-1-one;
- 4-(2-Methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
- 4-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-propyl-4,5-dihydro-1H-imidazole;
- 10 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
- 5,5-Dimethyl-2-[2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
- 15 N-(5-Bromo-2-methoxy-benzyl)-N'-methyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-N,N,N'-trimethyl-benzamidine;
- 20 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
- 1-Benzyl-2-{2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;
- {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-pyrrolidin-1-yl-methylene)-methyl-amine;
- 25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isopropyl-4,5-dihydro-1H-imidazole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-(2,2,2-trifluoro-ethyl)-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-
- 30 pyrimidine, and pharmaceutically acceptable salts thereof.

103. An MC4-R binding compound of the formula (IX):



(IX)

wherein:

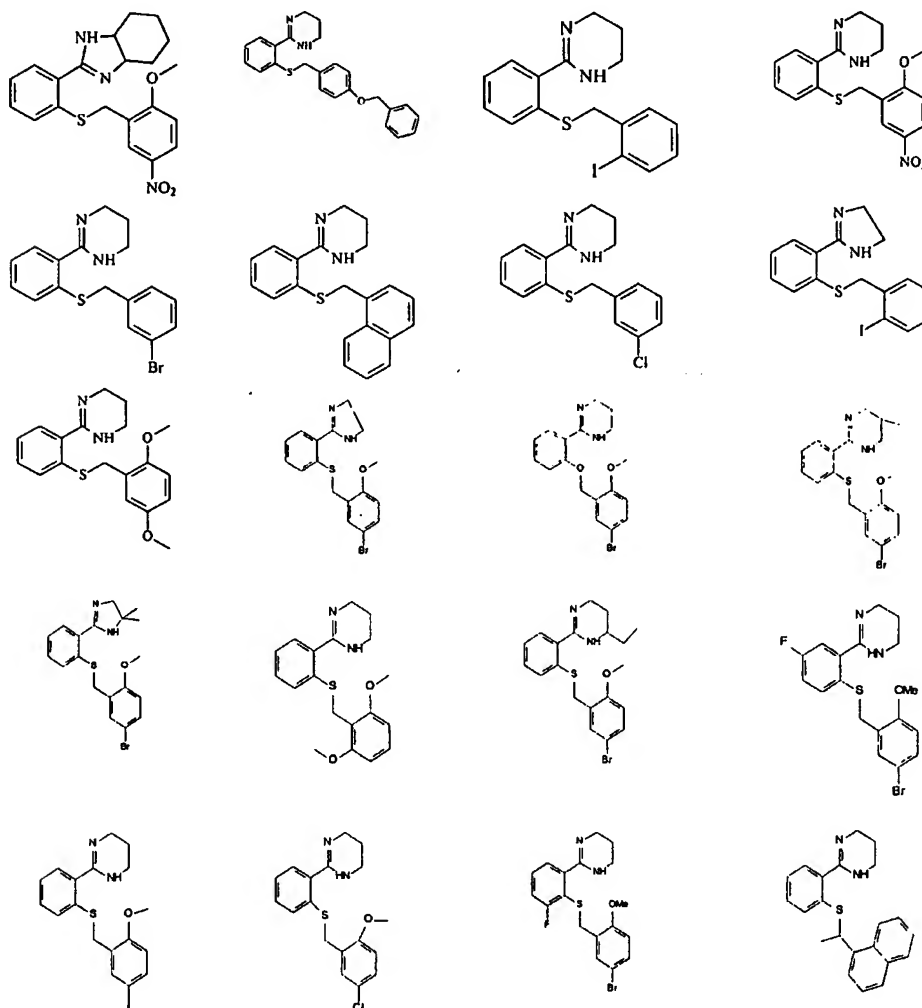
- 5 P² is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or
 a covalent bond;
 P³ is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, or Cl;
 P⁴ is CH, CCl, CBr, CF, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl or a
 sulfur atom;
 G¹ and G² are each independently CH₂, S, or O;
 10 r is a covalent bond or CH₂;
 t is CH₂, CHR³, or CR³R⁴;
 s is CH₂, CHR⁵ or CR⁵R⁶;
 R is hydrogen, alkyl, alkoxy, carbonyl, or alkylcarbonyl;
 Z¹ is CH, or covalently linked to Z² to form a naphthyl ring;
 15 Z² is CH, C-(C≡CH), CCl, CBr, Cl, CF, or covalently linked to Z¹ to
 form a naphthyl ring;
 Z⁵ is CH, or C-alkoxy;
 R³, R⁴, R⁵, and R⁶ are methyl, ethyl, hydroxyl, alkoxy, halogen, cyano,
 nitro, or amino, or pharmaceutically acceptable salts thereof.

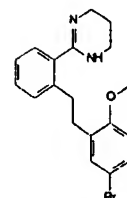
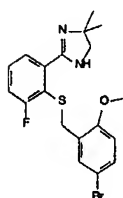
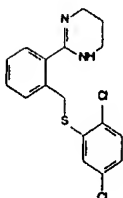
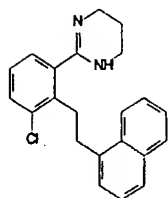
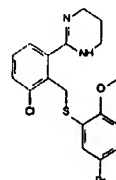
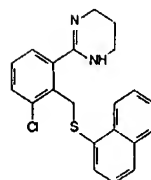
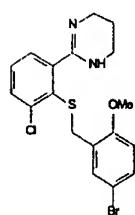
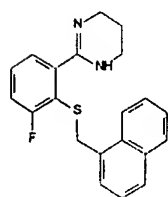
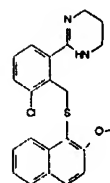
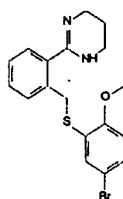
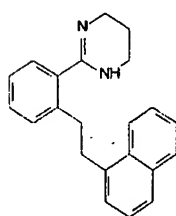
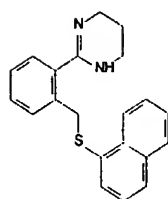
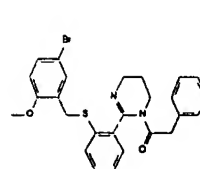
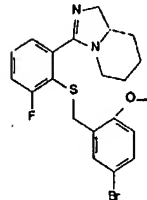
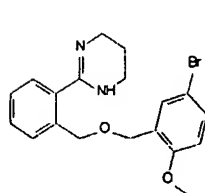
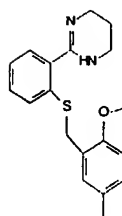
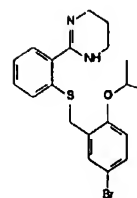
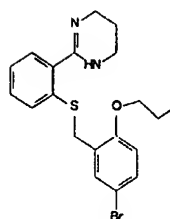
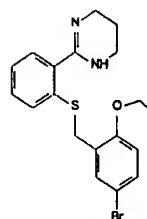
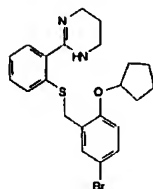
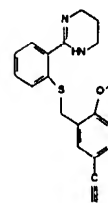
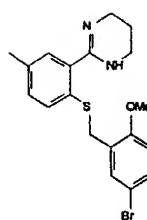
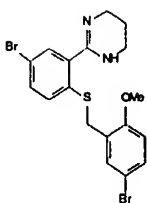
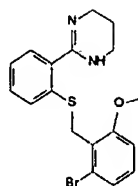
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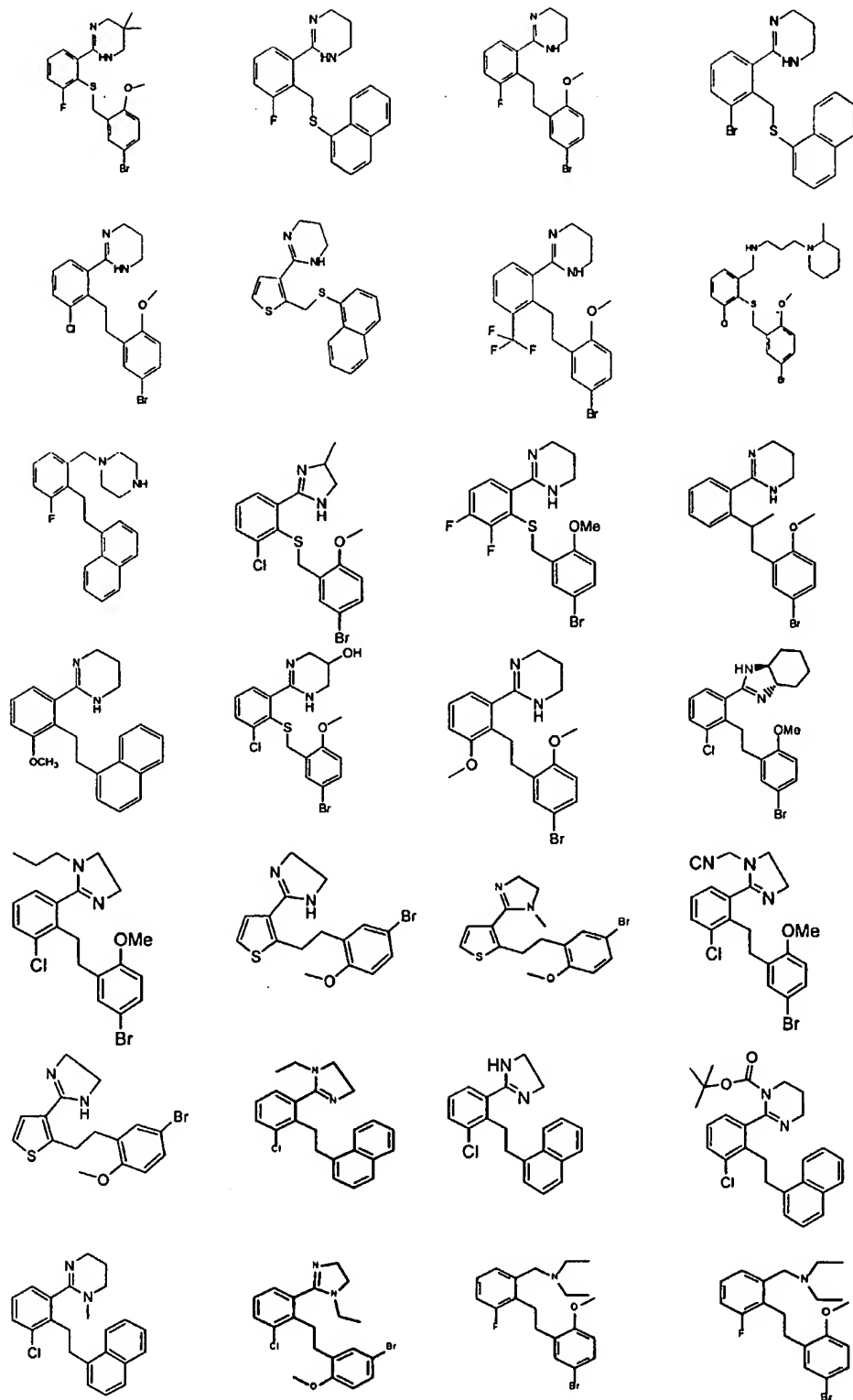
104. The compound of claim 103, wherein Z¹ is CH, Z² is CBr and Z⁵ is C-OMe.
105. The compound of claim 103, wherein P² is CH.
- 25 106. The compound of claim 103, wherein P⁴ is CCl or CF.
107. The compound of claim 103, wherein G¹ and G² are each CH₂.
108. The compound of claim 103, wherein G¹ and G² together are -CH₂-S- or -S-
 30 CH₂-.

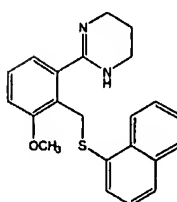
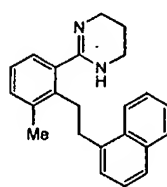
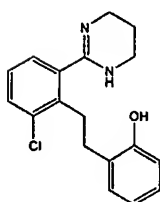
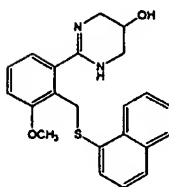
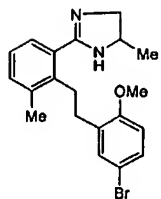
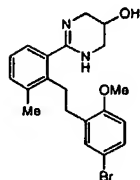
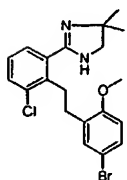
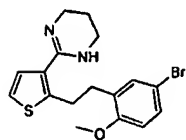
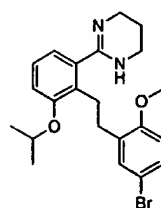
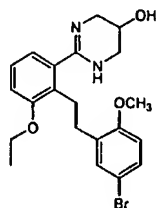
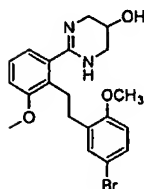
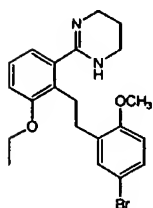
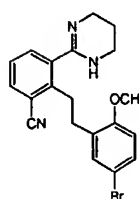
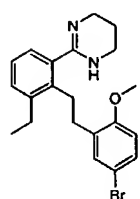
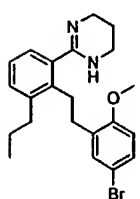
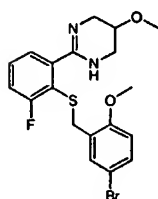
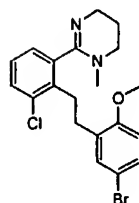
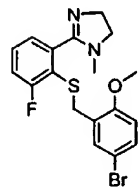
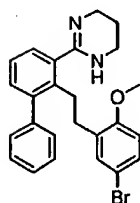
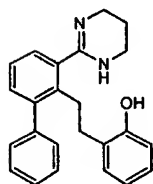
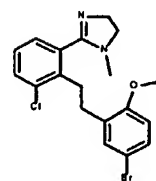
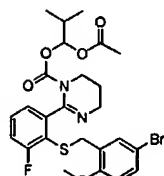
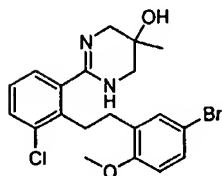
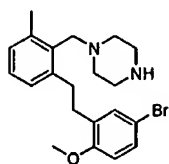
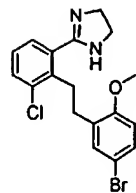
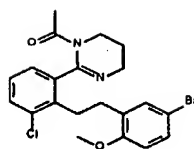
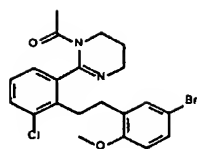
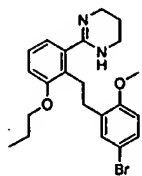
109. The compound of claim 103, wherein Z^1 and Z^2 are linked to form a naphthyl ring.
110. The compound of claim 103, wherein r is a covalent bond, s is R^5R^6 , and t is R^3R^4 , wherein each of R^3 , R^4 , R^5 and R^6 are each independently alkyl, hydroxy, or hydrogen.
111. An MC4-R binding compound or pharmaceutically acceptable salts thereof, wherein said compound is selected from the group consisting of:

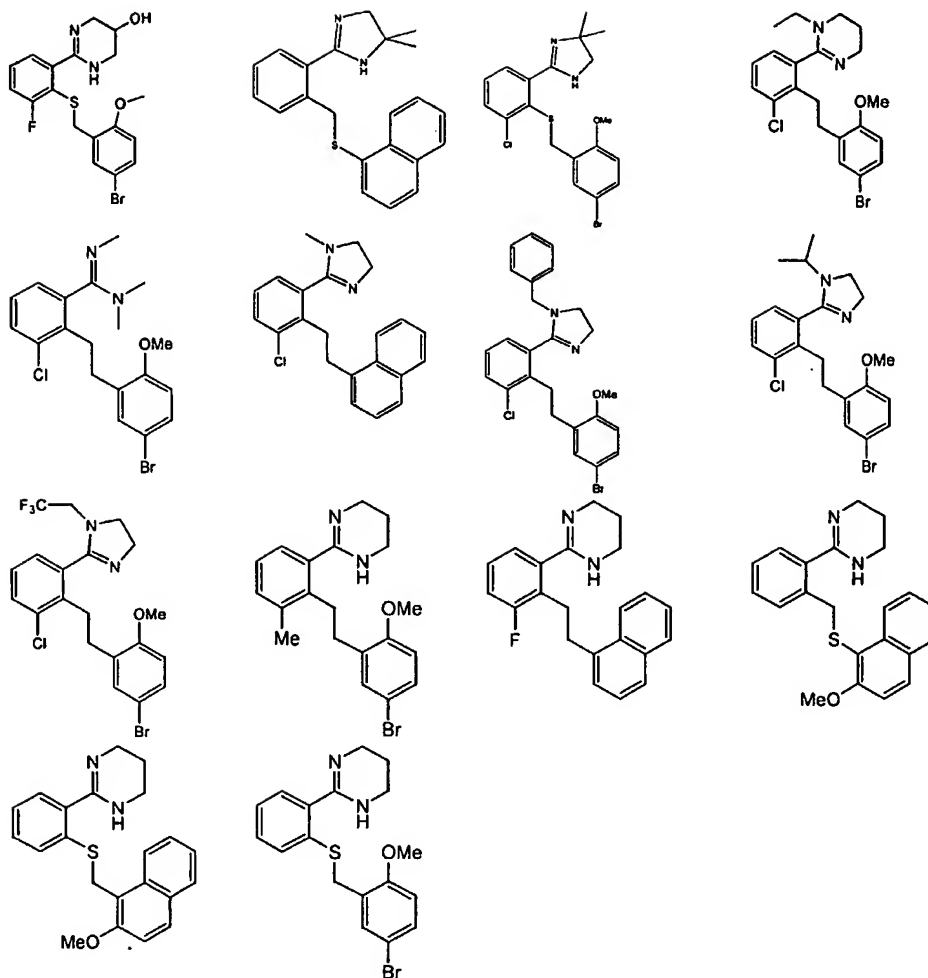
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112. A pharmaceutical composition for the treatment of a MC4-R associated state in a mammal comprising a pharmaceutically acceptable carrier and an effective amount of an MC4-R binding compound of the formula (I):

5

B-Z-E**(I)**

wherein

B is an anchor moiety;

Z is a central moiety;

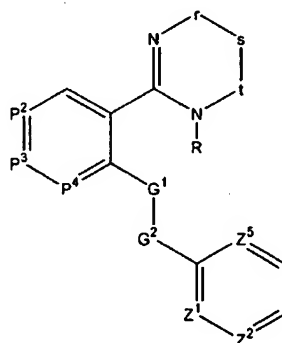
E is a MC4-R interacting moiety; and

pharmaceutically acceptable salts thereof.

10

113. The pharmaceutical composition of claim 112, wherein said MC4-R binding
15 compound is an MC4-R antagonist.

114. The pharmaceutical composition of claim 112, wherein said MC4-R associated state is associated with pigmentation.
115. The pharmaceutical composition of claim 112, wherein said MC4-R associated state is associated with weight loss.
116. The pharmaceutical composition of claim 115, wherein said weight loss is a result of old age, anorexia nervosa, HIV cachexia or cancer cachexia.
117. The pharmaceutical composition of claim 112, wherein said mammal is a human.
118. The pharmaceutical composition of claim 112, wherein said MC4-R binding compound is of the formula (IX):



(IX)

wherein:

- P^2 is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or a covalent bond;
- P^3 is CH, CF, CCl, CBr, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, or Cl;
- P^4 is CH, CCl, CBr, CF, C-alkyl, C-aryl, C-alkoxy, C-CN, C-OH, Cl, or a sulfur atom;
- G^1 and G^2 are each independently CH_2 , S, or O;
- r is a covalent bond or CH_2 ;
- t is CH_2 , CHR^3 , or CR^3R^4 ;
- s is CH_2 , CHR^5 or CR^5R^6 ;
- R is hydrogen, alkyl, alkoxycarbonyl, or alkylcarbonyl;
- Z^1 is CH, or covalently linked to Z^2 to form a naphthyl ring;
- Z^2 is CH, C-(C \equiv CH), CCl, CBr, Cl, CF, or covalently linked to Z^1 to form a naphthyl ring;
- Z^5 is CH, or alkoxy;

R³, R⁴, R⁵, and R⁶ are methyl, ethyl, hydroxyl, alkoxy, halogen, cyano, nitro, or amino, or pharmaceutically acceptable salts thereof.

119. The pharmaceutical composition of claim 112, wherein said MC4-R binding
 5 compound is selected from the group consisting of: 2-[2-(4-benzyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 10 2-[2-(3-chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,5-dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-iodo-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 15 2-[2-(2-methoxy-5-nitro-benzyloxy)-phenyl]-1,4,5,6-tetrahydropyrimidine;
 2-[2-(2-bromo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-iodo-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-methoxy-5-nitro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
 20 2-{2-[2-(2-methoxy-naphthalen-1-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
 2-[2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
 2-{2-[2-(2-methyl-naphthalen-1-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
 2-{2-[2-(2,3-dihydro-benzo[1,4]dioxin-5-yl)-ethyl]-phenyl}-1,4,5,6-tetrahydropyrimidine;
 25 2-[2-(2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydropyrimidine;
 2-(2-Benzylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-(2-Pentadecylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-(2-Cyclohexylmethylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 30 2-[2-(3-Nitro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3,5-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(4-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Chloro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Fluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 35 2-[2-(2,4-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3,5-Bis-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-nitro-benzyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-(2-Benzylsulfanyl-phenyl)-4,5-dihydro-1H-imidazole;
 2-[2-(2,6-Difluoro-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(Naphthalen-1-ylmethoxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 5 2-[2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-{2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-
 ethanone;
 2-[2-(2-Chloro-6-fluoro-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-
 benzoimidazole;
 10 2-[2-(2-Iodo-benzylsulfanyl)-phenyl]-3a,4,5,6,7,7a-hexahydro-1H-benzoimidazole;
 2-[2-(2,5-Dimethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 4-[2-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-quinoline;
 2-[2-(2-Methoxy-5-nitro-benzylsulfanyl)-pyridin-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 15 2-[2-(2-Cyclopentylloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,3-Dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 pyrimidine;
 2-[2-(6-Methoxy-2,3-dihydro-benzo[1,4]dioxin-5-ylmethylsulfanyl)-phenyl]-1,4,5,6-
 tetrahydro-pyrimidine;
 20 2-[2-(5-fluoro-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 1-Methyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[2-(5-Bromo-2-methoxy-benzylloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(Naphthalen-1-ylloxymethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-
 pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-
 imidazole;
 2-[2-(2,6-Dimethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 30 2-[2-(2-Bromo-6-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-4,5-dihydro-1H-imidazole;
 2-[5-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 pyrimidine;
 2-[4-Bromo-2-(5-bromo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
 35 pyrimidine;
 2-[2-(2-Bromo-5-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methyl-phenyl]-1,4,5,6-tetrahydro-
 pyrimidine;

- 2-[2-(Biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Chloro-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-thiophen-3-yl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(Biphenyl-2-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Iodo-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-
- 10 pyrimidine;
 2-[2-(4,4'-Dimethoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(9H-Fluoren-9-ylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(3'-Chloro-4'-fluoro-4-methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-
- 15 tetrahydro-pyrimidine;
 2-[2-(1-Naphthalen-1-yl-ethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-fluoro-phenyl]-4,5-dihydro-1H-imidazole;
 2-(2-Benzhydrylsulfanyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2'-Fluoro-4"-methoxy-[1,1';4',1"]terphenyl-3"-ylmethylsulfanyl)-phenyl]-1,4,5,6-
- 20 tetrahydro-pyrimidine;
 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzamidine;
 2-[4-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Ethynyl-2-methoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;
- 25 2-[2-(5-Bromo-2-cyclopentyloxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-ethoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-propoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
- 30 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperazine;
 C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-morpholin-2-yl}-methylamine;
 2-[2-(2-Methoxy-5-methyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-benzylloxymethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 35 [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-dimethyl-amine;
 2-[2-(5-Bromo-2-isopropoxy-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Ethoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Propoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-benzonitrile;
 1-{4-Methoxy-3-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylsulfanylmethyl]-phenyl}-ethanone;
- 5 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;
 C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-methylamine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
- 10 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,5,6,7,8,8a-hexahydro-imidazo[1,5-a]pyridine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6,7,7a-tetrahydro-1H-pyrrolo[1,2-c]imidazole;
- 15 2-[2-(Benzo[b]thiophen-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Fluoro-2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-(Naphthalen-1-ylmethylsulfanyl)-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 20 2-[2-(2-Methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-3-methyl-butan-1-one;
 1-{2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-5,6-dihydro-4H-pyrimidin-1-yl}-2-phenyl-ethanone;
- 25 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyridin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 N-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-guanidine;
 2-[2-(2-Isopropoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Cyclopentyloxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-
- 30 pyrimidine;
 (5-Bromo-2-methoxy-benzyl)-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-
- 35 pyrimidine;
 2-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(6-Bromo-2-methoxy-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Chloro-2-(2-methoxy-naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[1-(2-Naphthalen-1-yl-ethyl)-1H-pyrrol-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 (5-Bromo-2-methoxy-benzyl)-methyl-[2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-amine;
- 2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamine;
- 2-[2-(2-Chloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Bromo-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-(2-o-Tolylsulfanylmethyl-phenyl)-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2,5-Dichloro-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-(3-Amino-propylamino)-6-(5-bromo-2-methoxy-benzylsulfanyl)-benzonitrile;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-1,4,5,6-tetrahydro-pyrimidine;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-diethyl-amine;
- 20 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-morpholine;
- 3'-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyrazinyl;
- 2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-piperazin-1-yl-6,7-dihydro-quinoxaline;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidine;
- C-{4-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-morpholin-2-yl}-
- 25 methylamine;
- 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-pyrrolidin-3-ylamine;
- 1-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-quinoxalin-2-yl]-pyrrolidin-3-ylamine;
- 1-[2-(2-Methoxy-naphthalen-1-ylmethylsulfanyl)-benzyl]-pyrrolidin-3-ylamine;
- C-{4-[3-(5-Bromo-2-methoxy-benzylsulfanyl)-pyrazin-2-yl]-morpholin-3-yl}-
- 30 methylamine;
- 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-azetidine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ol;
- [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl
- 35 ester;
- [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester;

- [2-(2-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-ethyl ester;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-2-yl}-methanol;
- 5 4-tert-Butyl-N-naphthalen-1-ylmethyl-N-(2-piperidin-1-yl-ethyl)-benzamide;
 N,N-Dimethyl-N'-naphthalen-2-ylmethyl-N'-naphthalen-1-ylmethyl-propane-1,3-diamine;
 N-(5-Bromo-2-methoxy-benzyl)-N',N'-dimethyl-N-naphthalen-1-ylmethyl-propane-1,3-diamine;
- 10 1-Naphthalen-1-ylmethyl-3-phenethyl-1-(2-piperidin-1-yl-ethyl)-thiourea;
 3-(4-Dimethylamino-phenyl)-1-(3-dimethylamino-propyl)-1-naphthalen-1-ylmethyl-thiourea;
 4-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzylamino]-piperidine-1-carboxylic acid ethyl ester;
- 15 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethylamine;
 Naphthalene-2-sulfonic acid (2-dimethylamino-ethyl)-naphthalen-1-ylmethyl-amide;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-2-methoxymethyl-pyrrolidine;
 (2-Hexyloxy-phenyl)-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester;
- 20 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-pyrrolidine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-piperidine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-propan-1-ol;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzylamino]-3-methyl-butan-1-ol;
- 25 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-3-ol;
 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-pyrrolidin-2-yl}-methanol;
 {1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 2-[2-(Naphthalen-1-ylsulfanylmethyl)-pyrrolidin-1-yl]-ethyl-N-pyrrolidine;
 N-pyrrolyl-[1-(2-naphthalen-1-yl-ethyl)-pyrrolidin-2-ylmethyl]-amine;
- 30 1-(2-Naphthalen-1-yl-ethyl)-piperidine-2-carboxylic acid methyl ester;
 (3-Bromo-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-amine;
 3-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxy]-piperidine;
 (5-Bromo-2-methoxy-benzyl)-(1-ethyl-pyrrolidin-2-ylmethyl)-naphthalen-1-ylmethyl-amine;
- 35 (1-Ethyl-pyrrolidin-2-ylmethyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyloxymethyl]-pyrrolidine;
 (3-Bromo-benzyl)-(3-imidazol-1-yl-propyl)-naphthalen-1-ylmethyl-amine;
 (3-Imidazol-1-yl-propyl)-naphthalen-2-ylmethyl-naphthalen-1-ylmethyl-amine;

- [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-piperidin-1-yl-1-piperidin-1-ylmethyl-ethyl ester;
 [2-(Naphthalen-1-ylmethylsulfanyl)-phenyl]-carbamic acid 2-dimethylamino-ethyl ester;
 1-[2-(Naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 5 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-amine;
 1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperazine;
 N,N-Dimethyl-N'-(2-naphthalen-1-yl-ethyl)-N'-naphthalen-1-ylmethyl-ethane-1,2-diamine;
 10 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 1-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-benzyl]-piperazine;
 {1-[3-Chloro-2-(naphthalen-1-ylsulfanylmethyl)-benzyl]-piperidin-2-yl}-methanol;
 15 {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperidin-2-yl}-methanol;
 {1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-piperidin-2-yl}-methanol;
 [3-(2-Methyl-piperidin-1-yl)-propyl]-[2-(2-naphthalen-1-yl-ethyl)-benzyl]-amine;
 1-[2-(2-Naphthalen-1-yl-ethyl)-benzyl]-pyrrolidin-3-ylamine;
 1-Phenyl-3-piperazin-1-yl-5,6,7,8-tetrahydro-isoquinoline-4-carbonitrile;
 20 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(4-Methoxy-biphenyl-3-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2-Methoxy-5-phenylethynyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 25 2-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-(2-Methoxy-naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(2,5-Dimethoxy-phenylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(4-Methyl-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 30 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,5-dimethyl-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-(Naphthalen-1-ylsulfanylmethyl)-thiophen-2-yl]-1,4,5,6-tetrahydro-pyrimidine;
 35 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-phenyl}-1,4,5,6-tetrahydro-pyrimidine;

- 2-[2-(5-Bromo-2-methoxy-phenylsulfanylmethyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-[3-Bromo-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Methoxy-5-trifluoromethyl-benzylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-[4-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(Naphthalen-1-ylsulfanylmethyl)-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-trifluoromethyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(2-Naphthalen-1-yl-ethyl)-3-trifluoromethyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-[2-(6-Fluoro-naphthalen-1-ylmethylsulfanyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- {1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-piperidin-2-yl}-methanol;
- 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-[3-(2-methyl-piperidin-1-yl)-propyl]-amine;
- 20 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-pyrrolidin-3-ylamine;
- 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-benzyl]-piperazine;
- 5,5-Dimethyl-2-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
- 2-[3-Fluoro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 25 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,5-difluoro-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 3-(2-Naphthalen-1-yl-ethyl)-2-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenylamine;
- 30 Amino-[2-(2-naphthalen-1-yl-ethyl)-phenyl]-acetonitrile;
- 1-[2-(2-Naphthalen-1-yl-ethyl)-phenyl]-ethane-1,2-diamine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;
- 35 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4-methyl-4,5-dihydro-1H-imidazole;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Fluoro-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-5,5-dimethyl-4,5-dihydro-1H-imidazole;
- 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-1-methyl-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
- 2-[2-(5-Bromo-2-methoxy-benzyl sulfanyl)-3-fluoro-4-trifluoromethyl-phenyl]-5,5-
- 10 dimethyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[3-Methoxy-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-
- 15 pyrimidine;
- 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-chloro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
- 2-[2-(1-Methyl-2-naphthalen-1-yl-ethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 3-(5-Bromo-2-methoxy-benzylsulfanyl)-2-fluoro-4-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-
- 20 phenylamine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 25 1-Amino-3-[2-(5-bromo-2-methoxy-phenyl)-7-fluoro-benzo[b]thiophen-3-ylamino]-propan-2-ol;
- 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1,4,5,6-tetrahydro-
- 30 pyrimidin-5-ol;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-5-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-Chloro-6-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-phenyl]-ethyl}-phenol;
- 2-[3-Methoxy-2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-1,4,5,6-tetrahydro-pyrimidin-
- 35 5-ol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-5-methyl-4,5-dihydro-1H-imidazole;

- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methyl-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3,4-difluoro-phenyl]-1,4,5,6-tetrahydro-pyrimidin-5-ol;
5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,4-dimethyl-4,5-dihydro-1H-imidazole;
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-4-methyl-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
4,4-Dimethyl-2-[2-(naphthalen-1-ylmethylsulfanyl)-phenyl]-4,5-dihydro-oxazole;
10 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-4-methoxy-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
2-[5-(5-Bromo-2-methoxy-benzyl)-2-methyl-thiophen-3-yl]-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1,4,5,6-tetrahydro-
15 pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
20 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isopropoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-methoxy-phenyl}-1,4,5,6-tetrahydro-
25 pyrimidin-5-ol;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-methoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
30 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(1,4,5,6-tetrahydro-pyrimidin-2-yl)-benzonitrile;
2-{3-Benzyloxy-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-4-butyl-phenyl}-1,4,5,6-tetrahydro-
35 pyrimidine;
2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;

- 2-{5-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-8-chloro-2,3-dihydro-benzo[1,4]dioxin-6-yl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-ethyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propyl-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-isobutoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 10 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-butoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5-methoxy-1,4,5,6-tetrahydro-pyrimidine;
- 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-1,4,5,6-tetrahydro-pyrimidine;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
- [2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
- 20 2-{2-[3-(1,4,5,6-Tetrahydro-pyrimidin-2-yl)-biphenyl-2-yl]-ethyl}-phenol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-methyl-4,5-dihydro-1H-imidazole;
- N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methoxy-benzamide;
- 25 N-(3-Amino-propyl)-2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzamide;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-2-methyl-propyl ester;
- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-fluoro-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 30 3-(5-Bromo-2-methoxy-phenyl)-5-chloro-3,4-dihydro-isoquinolin-1-ylamine;
- 2-[2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-(4-methoxy-benzyloxy)-phenyl]-1,4,5,6-tetrahydro-pyrimidine;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5-methyl-1,4,5,6-tetrahydro-pyrimidin-5-ol;
- 35 2-[(5-Bromo-2-methoxy-phenyl)-(3-piperidin-1-yl-propylamino)-methyl]-3-chloro-6-methyl-phenol;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-4-methyl-piperazine;

- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-methyl-benzyl}-diethyl-amine;
 3-(5-Bromo-2-methoxy-phenyl)-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 5 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;
 10 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-methanol;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
 15 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
 20 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
 25 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
 (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidin-2-yl)-methanol;
 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-benzamide;
 30 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-4-methyl-piperazine;
 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidine;
 35 {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-diethyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-1H-imidazole;

- (1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-benzyl}-piperidin-2-yl)-methanol;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-propoxy-phenyl}-1,4,5,6-tetrahydro-pyrimidine;
- 5 1-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-benzyl]-4-methyl-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-4-methyl-piperazine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-piperidine;
- {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-6-chloro-benzyl}-diethyl-amine;
- 10 1-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid 1-acetoxy-ethyl ester;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-ethanone;
- 15 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-4-methyl-piperazine;
- {2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-diethyl-amine;
- 1-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-fluoro-benzyl}-piperidine;
- 4-Fluoro-N-{2-[4-(2-methoxy-phenyl)-piperazin-1-yl]-ethyl}-N-pyridin-2-yl-benzamide;
- 20 3-(5-Bromo-2-methoxy-phenyl)-2-methyl-1,2,3,4-tetrahydro-isoquinoline;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-4,5-dihydro-1H-imidazole;
- {2-[3-(5-Bromo-2-methoxy-phenyl)-3,4-dihydro-1H-isoquinolin-2-yl]-ethyl}-diethyl-amine;
- 25 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazol-1-yl)-ethanone;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-
- 30 1-carboxylic acid isobutyl ester;
- 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
- 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-imidazol-1-yl)-2,2-dimethyl-propan-1-one;
- 35 1-(5-Bromo-2-methoxy-benzyl)-2,3-dihydro-1H-isoindole;
- 1-(2-Methoxy-benzyl)-2-methyl-2,3-dihydro-1H-isoindole;
- 2-Methyl-1-naphthalen-1-ylmethyl-2,3-dihydro-1H-isoindole;

- 1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-2,2-dimethyl-propan-1-one;
 {2-[1-(5-Bromo-2-methoxy-benzyl)-1,3-dihydro-isoindol-2-yl]-ethyl}-diethyl-amine;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-1,4,5,6-tetrahydro-
 5 pyrimidine;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-5,6-dihydro-4H-pyrimidine-1-carboxylic acid tert-butyl ester;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-1H-imidazole;
 1-{2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazol-1-yl}-
 10 ethanone;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid isobutyl ester;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid tert-butyl ester;
 15 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-4,5-dihydro-imidazole-1-carboxylic acid ethyl ester;
 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-N-(3-formylamino-propyl)-6-methyl-benzamide;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-ethyl-4,5-dihydro-1H-imidazole;
 20 1-(2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidin-1-yl)-2,2-dimethyl-propan-1-one;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-4,5-dihydro-1H-imidazole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-5,6-dihydro-4H-pyrimidine-1-carboxylic acid isobutyl ester;
 25 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isocyanomethyl-4,5-dihydro-1H-imidazole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-methyl-4,5-dihydro-1H-imidazole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-thiophen-3-yl}-1-ethyl-4,5-dihydro-1H-
 30 imidazole;
 3-(5-Bromo-2-methoxy-benzyl)-2-methyl-2,3-dihydro-isoindol-1-one;
 4-(2-Methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
 4-(5-Bromo-2-methoxy-benzyl)-2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinoline;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-propyl-4,5-dihydro-
 35 1H-imidazole;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-3a,4,5,6,7,7a-hexahydro-1H-benzimidazole;
 5,5-Dimethyl-2-[2-(naphthalen-1-ylsulfanylmethyl)-phenyl]-4,5-dihydro-1H-imidazole;

- 2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-3-chloro-phenyl]-4,4-dimethyl-4,5-dihydro-1H-imidazole;
 N-(5-Bromo-2-methoxy-benzyl)-N'-methyl-N-naphthalen-1-ylmethyl-ethane-1,2-diamine;
 5 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-ethyl-1,4,5,6-tetrahydro-pyrimidine;
 2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-N,N,N'-trimethyl-benzamidine;
 2-[3-Chloro-2-(2-naphthalen-1-yl-ethyl)-phenyl]-1-methyl-4,5-dihydro-1H-imidazole;
 1-Benzyl-2-{2-[2-(5-bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-4,5-dihydro-
 10 1H-imidazole;
 ({2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-pyrrolidin-1-yl-methylene)-methyl-amine;
 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-isopropyl-4,5-dihydro-1H-imidazole;
 15 2-{2-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-3-chloro-phenyl}-1-(2,2,2-trifluoro-ethyl)-4,5-dihydro-1H-imidazole;

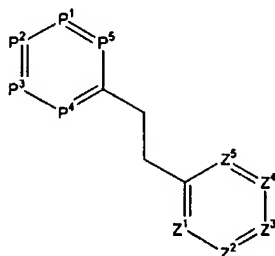
2-[2-(5-Bromo-2-methoxy-benzylsulfanyl)-phenyl]-6-ethyl-1,4,5,6-tetrahydro-pyrimidine, and pharmaceutically acceptable salts thereof.

20

120. The pharmaceutical composition of claim 112, wherein said pharmaceutical composition is suitable for oral administration.

121. The MC4-R binding compound of the formula (VII):

25



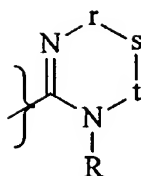
(VII)

wherein

Z^1 , Z^2 , Z^3 , Z^4 , and Z^5 are CH, N, or substituted carbon;

P^1 , P^2 , P^3 , and P^4 are CH, N or substituted carbon; and

30 P^5 is C-J, wherein J is a moiety of the formula (XIII):



(XIII)

wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

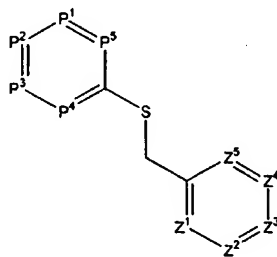
t is CH, CH₂, CHR³, CR³R⁴, or H;

5 s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;

R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxy, carbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and

10 R¹, R², R³, R⁴, R⁵, and R⁶ are each independently halogen, thiol, thioalkyl, thioester, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl, optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

122. The MC4-R binding compound of the formula (VIII):



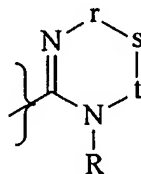
(VIII)

wherein

Z¹, Z², Z³, Z⁴, and Z⁵ are CH, N, or substituted carbon;

P¹, P², P³, and P⁴ are CH, N or substituted carbon; and

P⁵ is C-J, wherein J is a moiety of the formula (XIII):



(XIII)

wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

t is CH, CH₂, CHR³, CR³R⁴, or H;

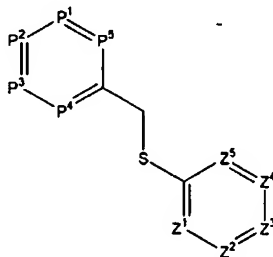
s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;

R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and

5. R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioether, thioalkyl, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl, optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

123. The MC4-R binding compound of the formula (XV):

10



(XV)

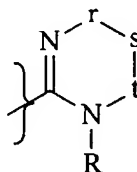
wherein

Z¹, Z², Z³, Z⁴, and Z⁵ are CH, N, or substituted carbon;

P¹, P², P³, and P⁴ are CH, N or substituted carbon; and

15

P⁵ is C-J, wherein J is a moiety of the formula (XIII):



(XIII)

wherein

r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;

t is CH, CH₂, CHR³, CR³R⁴, or H;

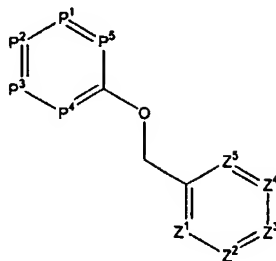
20

s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;

R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxycarbonyl, arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form one or more rings; and

- 25 R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioether, thioalkyl, alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl, optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

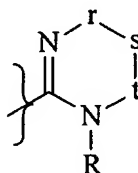
124. The MC4-R binding compound of the formula (XVI):



(XVI)

wherein

- 5 Z^1, Z^2, Z^3, Z^4 , and Z^5 are CH, N, or substituted carbon;
 P^1, P^2, P^3 , and P^4 are CH, N or substituted carbon; and
 P^5 is C-J, wherein J is a moiety of the formula (XIII):



(XIII)

wherein

- 10 r is a covalent bond, CH, CH₂, CHR¹, CR¹R², or H;
 t is CH, CH₂, CHR³, CR³R⁴, or H;
 s is CH, CH₂, CHR⁵, CR⁵R⁶, or absent;
 R is hydrogen, alkyl, alkenyl, arylalkyl, arylcarbonyl, alkoxy, carbonyl,
 arylalkylcarbonyl, alkylcarbonyl, optionally linked to R¹, R², R³, R⁴, R⁵, or R⁶ to form
 15 one or more rings; and
 R¹, R², R³, R⁴, R⁵, and R⁶ are each halogen, thiol, thioether, thioalkyl,
 alkoxy, alkyl, alkenyl, alkynyl, heterocyclic, hydroxyl, nitro, amino, cyano, aryl,
 optionally linked to form a ring with R, R¹, R², R³, R⁴, R⁵, or R⁶.

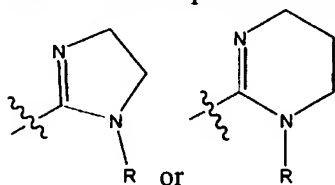
- 20 125. The compound of any one of claims 121-124, wherein P¹, P², P³, and P⁴ are each substituted or unsubstituted carbon.

126. The compound of claim 125, wherein P¹ is CH.

- 25 127. The compound of claims 121-124, wherein at least one of P², P³ and P⁴ is substituted carbon.

128. The compound of any one of claims 121-124, wherein P^2 , P^3 and P^4 are each independently selected from the group consisting of CH, CF, Cl, CBr, C-alkyl, C-alkoxy, C-aryl, and Cl.
- 5 129. The compound of any one of claims 121-124, wherein Z^3 and Z^4 are each CH.
130. The compound of any one of claims 121-124, wherein Z^1 is CH.
131. The compound of any one of claims 121-124, wherein Z^1 is covalently linked to
10 Z^2 to form a naphthyl ring.
132. The compound of any one of claims 121-124, wherein Z^2 is CH, C-(C \equiv CH), CCl, CBr, Cl, or CF.
- 15 133. The compound of any one of claims 121-124, wherein L_2 is a covalent bond.
134. The compound of any one of claims 121-124, wherein R is H, alkyl, arylcarboxy, alkylcarboxy, or arylalkylcarboxy.
- 20 135. The compound of any one of claims 121-124, wherein s is CR 5 R 6 and R 5 and R 6 are each methyl.
136. The compound of any one of claims 121-124, wherein r is a covalent bond.
- 25 137. The compound of any one of claims 121-124, wherein t, r and s are CH $_2$.

138. The compound of claim 121, wherein J is



wherein R is alkyl or hydrogen.

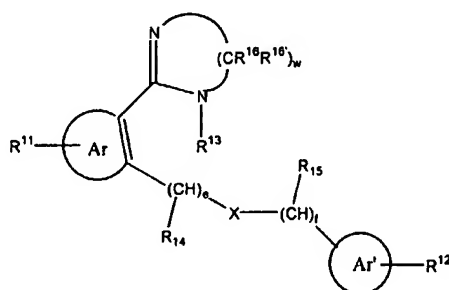
30

139. The compound of claim 138, wherein R is methyl, ethyl, or propyl.
140. The compound of any one of claims 121, 138 or 139, wherein P^1 , P^2 , and P^3 are each CH, and P^4 is CCl.

141. The compound of claim 121, wherein Z^1 , Z^3 , and Z^4 are each CH, Z^5 is COMe, and Z^2 is CBr.

5 142. The compound of claim 121, wherein Z^1 is covalently linked to Z^2 to form a naphthyl ring, and Z^3 , Z^4 and Z^5 are each CH.

143. An MC4-R binding compound of the formula (XVIII):



(XVIII)

wherein

Ar and Ar' are aromatic groups;

R^{11} is selected independently for each position capable of substitution from the group hydrogen, cyano, alkoxy, nitro, halogen, alkyl, amino, or aryloxy;

15 R^{12} is selected for each position capable of substitution from the group consisting of hydrogen, halogen, alkoxy, acetylenic, nitro, aryl, alkyl, alkenyl, alkynyl, cyano, acyl, or carbonyl;

R^{13} is hydrogen, alkenyl, alkynyl, aralkyl, nitro, cyano, alkyl, acyl, carbonyl, or SO_2CH_3 , and may optionally be linked to an R^{16} or an $R^{16'}$ group;

20 R^{16} and $R^{16'}$ are each independently selected for each position capable of substitution from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, hydroxyl, cyano, aryl, heterocyclic, carbonyl, or acyl, and may optionally be connected through an alkyl chain to R^{13} or another R^{16} or $R^{16'}$ group, to form a fused or spiro ring system;

X is NR^{17} , S, O or a covalent bond;

25 R^{17} is hydrogen, alkyl, or carbonyl;

R^{14} and R^{15} are each independently hydrogen, halogen, or alkyl;

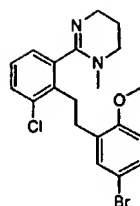
w is 1, 2, 3, or 4;

e is 0 or 1;

f is 0 or 1, wherein both e and f are not both 0 if X is a covalent bond,

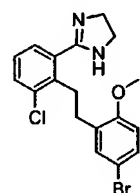
30 and pharmaceutically acceptable salts thereof.

144. The compound of the formula:



or a pharmaceutically acceptable salt thereof.

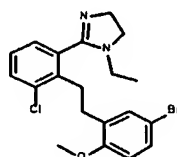
5 145. The compound of the formula:



or a pharmaceutically acceptable salt thereof.

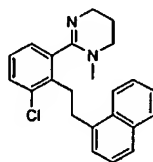
146. The compound of the formula:

10



or a pharmaceutically acceptable salt thereof.

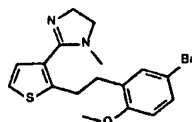
147. The compound of the formula:



15

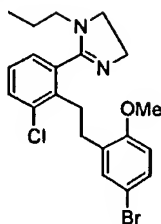
or a pharmaceutically acceptable salt thereof.

148. The compound of the formula:



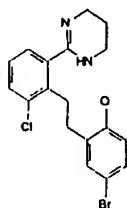
20 or a pharmaceutically acceptable salt thereof.

149. The compound of the formula:



or a pharmaceutically acceptable salt thereof.

5 150. The compound of the formula:



or a pharmaceutically acceptable salt thereof.

151. A method for treating a MC4-R associated state in a mammal comprising
10 administering an effective amount of a compound to a mammal, such that the MC4-R
associated state is treated, wherein said compound is any one of the compounds of
claims 144-150.

152. A method for treating a disorder associated with pigmentation or weight loss,
15 comprising administering an effective amount of a compound of any one of claims 144-
150.

153. The method of claim 152, wherein said effective amount is effective to treat a
disorder associated with pigmentation, weight loss, or bones.

20

154. The method of claim 153, wherein said weight loss is a result of anorexia
nervosa, old age, cancer cachexia, or HIV cachexia.

155. The method of claim 153, wherein said bone associated disorder is selected from
25 the group consisting of osteogenesis imperfecta, hypophosphatasia, Paget's disease,
fibrous dysplasia, osteopetrosis, osteoporosis, myeloma bone disease, the depletion of
calcium in bone, and bone fracture.

156. A pharmaceutical composition for the treatment of a MC4-R associated state in a mammal comprising a pharmaceutically acceptable carrier and an effective amount of an compound of any one of claims 144-150.
- 5 157. The method of any one of claims 1, 14, 65, 73, 74, 90, 101, or 102 wherein said MC4-R associated state is a bone associated state.
158. The method of claim 157, wherein said bone associated state is osteogenesis imperfecta, hypophosphatasia, Paget's disease, fibrous dysplasia, osteopetrosis,
10 myeloma bone disease, the depletion of calcium in bone, bone remodelling associated state or bone fracture.
159. The method of claim 157, wherein said bone associated state is osteoporosis.
- 15 160. A pharmaceutical composition of claim 112, wherein said effective amount is effective to treat a bone associated disorder.
161. The pharmaceutical composition of claim 160, wherein said bone associated disorder is osteogenesis imperfecta, osteoporosis, hypophosphatasia, Paget's disease,
20 fibrous dysplasia, osteopetrosis, myeloma bone disease, the depletion of calcium in bone, or bone fracture.

1/2

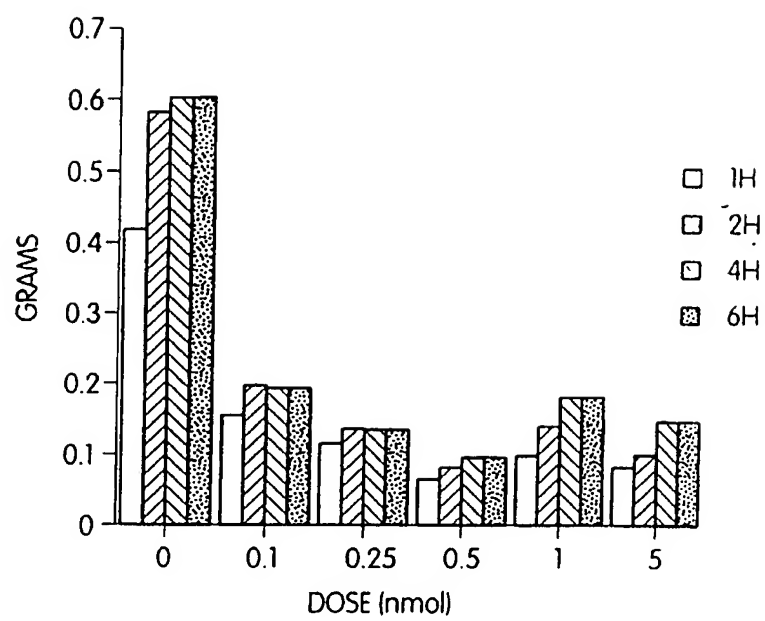


Fig. 1A

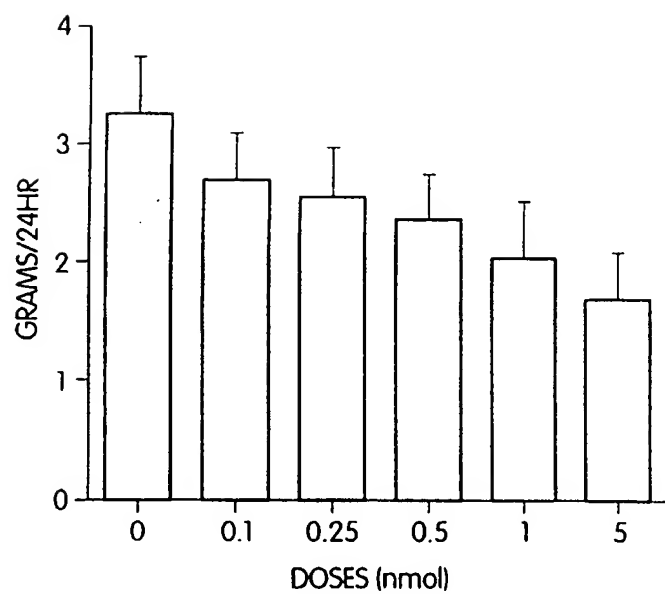


Fig. 1B

2/2

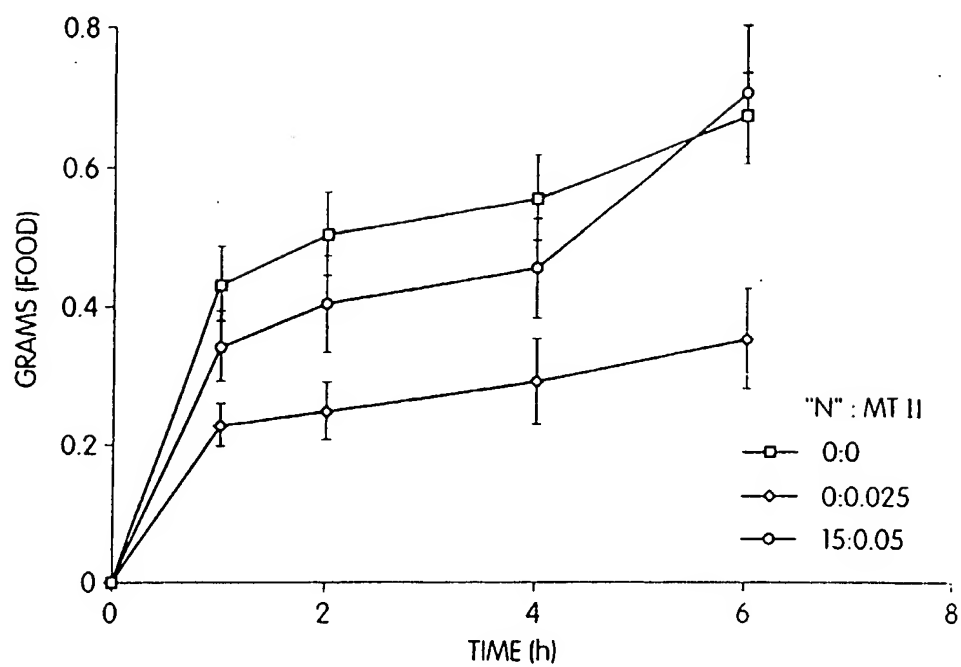


Fig. 2

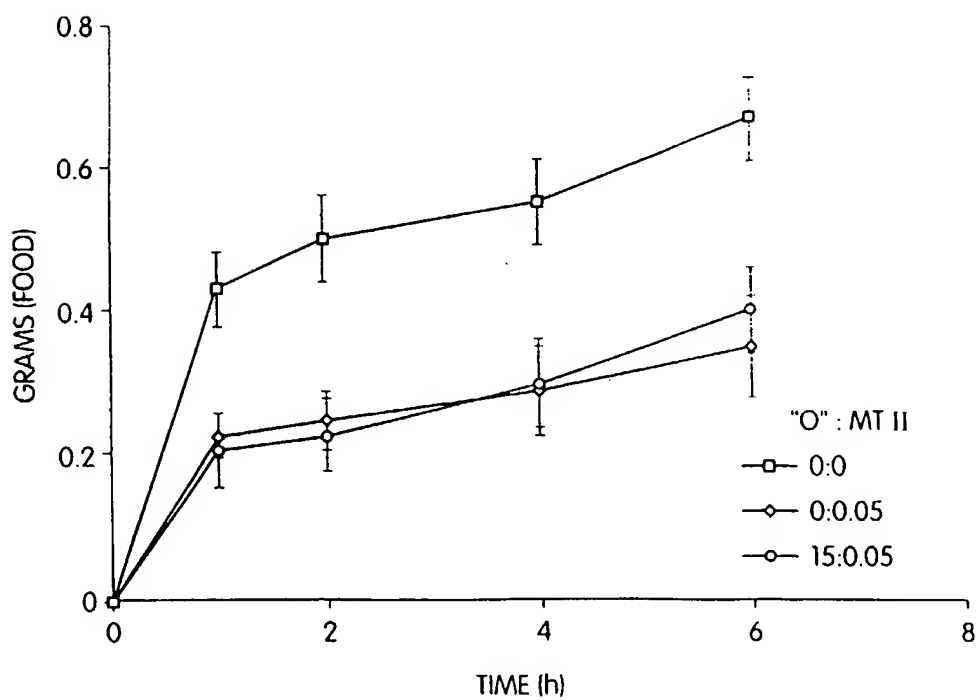


Fig. 3

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WO 02/062766 A3

(54) Title: MELANOCORTIN-4 RECEPTOR BINDING COMPOUNDS AND METHODS OF USE THEREOF

(57) Abstract: MC4-R binding compounds of the formula: B-Z-E (I) wherein B is an anchor moiety, Z is a central moiety, and E is a MC4-R interacting moiety are discussed. Methods of using the compounds to treat MC4-R associated disorders, such as disorders associated with weight loss, are also discussed.

INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER

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B. FIELDS SEARCHED

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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
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C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | GB 1,418,053 A (BADISCHE ANILIN- & SODA-FABRIK AKTIENGESELLSCHAFT) 17 December 1975 (17.12.75), formula (I) and Examples 13-18. | 112-118 |
| X | US 5,731,408 A (HADLEY et al) 24 March 1998 (24.03.98), Examples IV, VI and Tables I-III. | 1, 14, 112-118 |
| X | WO 99/64002 A1 (MERCK & CO., INC.) 16 December 1999 (16.12.99), see entire document. | 1-7, 9-10, 112-117 |
| X, P | WO 01/10842 A2 (MILLENNIUM PHARMACEUTICALS, INC.) 15 February 2001 (15.02.01), see entire document. | 1-161 |

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